Professor Bennett
with best thanks & earnest wishes of the
Author.

(23)

CASES AND OBSERVATIONS

ILLUSTRATING

INFLAMMATORY EFFUSIONS

INTO THE

SUBSTANCE OF THE LUNGS,

PARTICULARLY

AS MODIFIED BY CONTAGIOUS FEVERS.

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SUBSTANCE OF THE LUNGS,

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In the following pages I purpose to direct the attention of the medical profession to some pathological conditions of the lungs which do not appear to have been previously observed with sufficient care. The morbid changes referred to consist in the exudation of *liquor sanguinis* from the minute blood-vessels—a phenomenon in regard to which the views of pathologists are still somewhat vague, whether it occurs as a general morbid change, or in those particular forms to which it is my intention at present to advert; for it must be admitted that they are as yet very imperfectly acquainted with the minute anatomical relations of the exuded matter, the circumstances under which it is generated, and the conditions which tend to modify the changes which the new substances undergo subsequent to their exudation.

* The above communication formed the substance of An Inaugural Dissertation presented to the Faculty of Medicine by the author on his graduation at the University of Edinburgh in 1848, and for which one of the gold medals was awarded to him by the Senatus Academicus.

My remarks upon this subject will be illustrated by a series of cases which lately came under my observation in the Royal Infirmary of Edinburgh, in the description of which it will be my object principally to direct the attention of the reader to the manner in which the exuded matter may be traced into the minutest parts of the pulmonary texture; the circumstances modifying the elementary forms which the exuded *liquor sanguinis* may assume during its organization; and the different stages of progression by which this morbid affection may terminate in resolution, in permanent organic mischief, or in death.

In the examination of a lung not presenting all the appearances of health, it is impossible to ascertain with the unaided eye whether or not the morbid degeneration it may have undergone is of the nature of exudation; and still less to determine the nature of the exuded matter without the employment of the microscope.

In the lung, as in every other organ of the body subject to the exudation of *liquor sanguinis*, the matter resulting from the exudation is liable to various modifications, according to the structure of the part affected.

The question then presents itself at the outset of this inquiry; Under what circumstances is a lesion in the substance of the lung to be regarded as an exudation resulting from inflammatory action? Such a lesion will be found to exist when an exudation of *liquor sanguinis* has taken place and becomes organized in various forms; and it is my object to describe some of the conditions which appear to modify the forms of organization assumed by this exuded matter.

The coagulated matter of exudation exhibits in the pulmonary substance a general tendency to become organized, and it is only under more rare circumstances that it tends to undergo rapid disintegration or decomposition, and to involve the substance of the lung itself in death. Like other morbid processes, the organization of the exuded matter will be most conveniently considered with reference to its several stages; which have been well determined by Laennec. In the first stage, no exudation takes place; but the excess of blood in the part is followed by a serous effusion, and a decrease in the firmness of the parenchyma. This condition of hyperæmia appears to exist occasionally, under three circumstances. It may exist, (1) as the invariable condition of a part in which exudation of *liquor sanguinis* is about to take place; (2) as the result of deficient nervous energy, and the consequence of gravitation; (3) in the phenomena of blushing, and the vascularity of erectile tissues. A question here suggests itself, namely, "Is it possible to distinguish congestion in a part about to be the seat of an exudation of *liquor sanguinis*, from those other congestions which are stated to exist?" Almost

every author maintains that there is no ground of distinction sufficiently well-marked between the engorgement of inflammation in its first stage, and those congestions which I have specified. Andral considers the anatomical characters of hyperæmia as the same in all cases, so that the nature of the lesion found on dissection is only to be judged of according to the nature of the symptoms during life,* an opinion in which Bouillaud† and Williams‡ coincide. Chomel,§ however, attaches more importance to the morbid appearances after death, and grounds his opinion as to the existence or non-existence of inflammation on the presence of softening in the texture of the lung, considering friability of the lung a sufficient ground of distinction between inflammation and congestion. But there are cases of disease in which conditions of the lung are observed presenting all the morbid appearance of inflammation to the naked eye at least, and to the other organs of the senses, so far as consolidation, non-crepitation, and friability are concerned; and in which during life neither physical signs nor constitutional symptoms indicate any departure from the normal condition; from which it appears that it may be difficult, if not impossible, to distinguish whether the appearances presenting themselves after death, depend simply on congestion, on effused blood, or on mucous and purulent formation. This is more particularly the case in that condition of the lung described as hæmorrhagic hepatization, "the pneumonia of the dying," a condition which frequently follows surgical operations, and where death takes place by way of asthenia. In hæmorrhagic hepatization, there is no organized exudation of blood-plasma, there is merely congestion and effusion of blood, which may undergo those changes to which effused blood is subject. The existence of friability along with the congested appearance is not conclusive, although it adds to the probability of the existence of exudation. Friability of all the textures is a constant consequence of typhus fever, when no exudation into organs has taken place, as well as of recent organized products of exudation from the blood-vessels in any part, and under any conditions. Again, a lung may be consolidated from distension of the air-tubes and pulmonary vesicles by the epithelium secreted from their lining membrane. In the lungs of cattle that have died from pulmonary disease, I have seen the air-tubes filled by a secretion from their lining membrane, extending into their most minute ramifications, and so tough, firm, and elastic, that it was perfectly moulded to the calibre of the bronchia, and could be drawn out, preserving a cast of the tube and its ramifications.

* Pathological Anatom. Trans. vol. xi. p. 509.
† Dict. de Med. et de Chirurgie Pratiques, t. xiii. p. 36.
‡ Cyclop. of Prac. Med., vol. iii. p. 409.
§ Dict. de Med. et Chirurgie Pratiques, tom. xvii.

Such a condition rendered the lung perfectly dense, independently of any exudation from its blood-vessels into its substance. These are circumstances which lead to fallacy in determining the nature of the lesion affecting the lung; and it must be of importance if microscopic observation, or any other mode of research, shall be found sufficient to establish a difference between condensation from inflammatory, and that from non-inflammatory congestion. The difference, however, has not yet been discovered; and if ever it shall be, its more early distinctive features may be sought for in a change of the blood itself.

In reviewing the various theories of inflammation, and the changes which are described to take place in the blood, it is impossible to avoid entertaining the notion that a peculiar dyscrasia exists, which is at once the cause of the constitutional disturbance, the local lesion, and the particular form in which the exudation from the blood-vessels may become organized. This dyscrasia may consist either in the blood containing a morbid material, or in its normal constitution being changed. The coalescing of the blood-corpuscles, and the formation of a buffy coat, have long been supposed to be appearances especially connected with an inflammatory state.

To this dyscrasia Piorry has given the name of "hæmatitis." It has also been shown by Andral and Gavarret, that, during inflammation, an excess of fibrin exists in the blood, and that the proportion is not only increased relatively to the blood-globules and other constituents, but also in proportion to the whole amount of this fluid in the body. It is farther supposed that the blood is more inclined to adhere to the surrounding parts, from the appearances presented in the vessels, and from the fact of the corpuscles also possessing this property in regard to each other; a phenomenon which some have conceived to depend upon a change in the relations of the attractive forces of an organic kind or others, subsisting between the several component parts of the blood and the surrounding textures. So much indeed is the healthy constitution of the blood affected during the existence of several acute diseases, that some are inclined to consider acute rheumatism, chorea,* and pericarditis,† to be dependent on a morbid condition of the blood. From all these circumstances I feel convinced, and it is my object in this paper to show, that during the progress of extensive exudations from the blood-vessels into any organ, a dyscrasia of the blood exists; that it is owing, in part, to the existence of some such dyscrasia that these exudations take place, the ultimate nature of whose organization may be

* Dr Begbie on Rheumatism and Chorea, p. 15.

† Dr Taylor on the Causes of Pericarditis, in 28th vol. of Royal Med. and Chirurg. Soc. Trans., 1845.

made apparent by microscopic examination after death; and that in the series of changes which take place in a part where exudation from the blood-vessels has occurred, the forms of organization depend as much upon the nature of the particular dyserasia which exists, as upon the stage of development at which the organization of the exuded *liquor sanguinis* has arrived at the period of examination.

The cases of which I have witnessed the dissections in the Edinburgh Royal Infirmary, in which consolidation of the substance of the lung mainly contributed to cause death, or in which no other local lesion was apparent after death sufficient to account for the fatal termination, have been 101 in number, and were observed from June 10, 1847, until March 13, 1848. Many more cases of pulmonary disease during that period in the same hospital proved fatal, but only 101 could be inspected after death. The following table presents a condensed analysis of the conditions under which the pulmonary lesion existed.

The lung was more or less condensed—

in 56 cases of fever (34 of typhus, 22 of fever other than typhus);
13 do. in which Bright's disease existed;
13 do. marked by a cachexia, indicated by habitual bad health, various local lesions, and attended by intemperance;
6 do. of fatty heart, hypertrophy, and softening of texture;
4 do. of tuberculosis;
2 do. of secondary deposits;
2 do. of variola and rubeola;
2 do. with no other apparent lesion;
2 do. where disease extended from neighbouring parts;
1 do. with softening of *corpus striatum.*

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Of these 101 cases of pulmonary condensation, 56 occurred during the progress of fever. Of these 56 cases, 34 occurred during the progress of typhus and 22 during the course of fever other than typhus, such as continued fever or synocha.

In ten of the cases where the condensation occurred during the progress of typhus fever, the lung was the only organ affected. In the remaining twenty-four, other organs besides the lung appeared to have been the seat of exudation from the blood-vessels. In twelve cases the spleen was affected, in seven the pleura, in five the intestines, in four the liver, in three the pericardium; in two the heart was soft and flabby to a marked degree; in one there was gangrene of the toes; and in one there was softening of the corpus striatum; and in this latter case, the lung was in a state of gangrene; in one there was extensive ulceration of the tonsils,

larynx, and glottis, requiring the operation of tracheotomy. Next to the lung, therefore, which was more or less condensed in all of these cases, the spleen seems to have suffered most frequently during the progress of fever, and the other organs in the order in which I have enumerated them.

Of the 101 cases, thirteen had Bright's disease of the kidneys, and exudations into other organs besides the lungs; thirteen were marked by a cachectic state of the body; six suffered from heart disease; four had tuberculosis; two were the subjects of secondary deposits after operations; two of variola and rubeola; and in two the exudation extended by continuity or contiguity of tissue; in one case there was softening of the corpus striatum; and in two cases there was no exudation except what was found existing in the lung.

The extensive prevalence of the lesions throughout the body is the most important feature brought out by such an analysis,—a feature sufficient of itself to maintain the probability that no immediate exciting cause can account for such extensive exudation into the most vital and important of the internal organs. In every case it might be possible to point out the existence of a pathological condition sufficient to indicate a state of the constitution capable of exercising an influence over the development of exudation from the blood-vessels, whether in the lung or in any other organ. Between the existence of an exudation, therefore, and the presence of any morbid conditions of the body, such as typhus fever, Bright's disease, synocha, synochus, or variola, we are to recognize the existence of the same relations; for in all of these conditions we have circumstantial evidence of a dyscrasia in the blood.

During Bright's disease, we know that a non-elimination of urea is a constant pathological condition; that during its course there is a great liability to the exudation of *liquor sanguinis* in various internal organs—a liability proportioned in some degree to the amount of adulteration which an imperfect action of the kidneys causes in the blood; and that these internal exudations of *liquor sanguinis* can be justly referred to the condition of the blood alone.

During the progress of typhus fever, it is known that there is also a great liability to exudation from the blood-vessels of various organs, more especially in the lungs, spleen, pleuræ, intestines, liver, and pericardium; that the occurrence of these exudations bears no proportion to the apparent severity of the fever; for, frequently, cases of intestinal lesions, as well as lesions of the lungs or spleen, are discovered after death, when no knowledge of their presence could have been obtained from symptoms existing during life; that no immediately exciting cause

can account for the exudation; and, lastly, that the number of parts affected, shows the universal nature of the cause. By considering a dyscrasia of the blood to be a cause, at once of the typhus fever and of the exudation, we are enabled to explain the occurrence of a series of symptoms, by such a theory, if they are not found associated either with the epileptic constitution, or with delirium tremens. I refer to the occurrence of convulsions, which almost invariably prove fatal, of which I have given the records of six cases occurring in the Infirmary during the month of February 1848. (See Monthly Journal of Medical Science for June 1848.)

There can, perhaps, be no better illustration brought forward of the association of exudation from the blood-vessels with a vitiated condition of the blood, than that which is afforded by the exudations occurring during the course of exanthematous diseases. In the condition of scarlatina we have an exudation in the throat, of which the fauces seem to be especially susceptible. In rubeola the lungs seem to be the most frequent seat of exudation; in variola the skin and the intestinal canal. These facts show that, where such exudations into external organs accompany such diseases, where a morbid condition of the blood evidently exists, the exudations must be ascribed in part to that universal and constitutional cause. The cases of secondary deposits, as well as of tuberculosis, in which an unnatural state of the blood exists, bear the most direct testimony in favour of this view. The character and amount of organization which the exuded matter attains must, therefore, also be examined in relation to the morbid condition of the blood; and I hope to be able to show that, as the blood departs from the healthy standard, so does the character of the exudation change; for the morbid state of the blood is to be regarded as the cause of the peculiarities in the inflammatory products. Again, if we look to the immediately-exciting causes of the exudation into the lung, we shall find that they are usually described as those which are also the immediately-exciting cause of Bright's disease, of typhus fever, of synocha, or of synochus. Inadequate clothing, cold, wet, or intemperance have been looked upon as the common cause of all; but how frequently do exposures to all vicissitudes fail in inducing disease, until a change not usually perceived predisposes the individual to morbific agencies? The change is a gradual one, commencing in the fluids of the body, and brought about under a combination of circumstances, which renders the individual no longer able to resist the influence of morbid causes. No two individuals being constituted alike, either in mind or body, the relation of any individual to the atmosphere and its changes cannot be precisely the same, at any given time. The operation of similar causes, therefore, must

exercise different effects upon all; and therefore it is found, that at certain periods a combination of circumstances occurs in one or in a number of individuals, arising from causes which have always been in operation, which combination of circumstances is different from all other combinations of circumstances which have existed at any period in the life of the individual, or history of the species. In the condition of the individual, and his relation to the surrounding elements in which he lives, are to be found those agencies, or that agency, which gives rise to a distemper of a new and unknown form. Thus far the disease is new, the agency or agencies new, unknown, and it may be invisible, because the combination of circumstances are novel, but the causes which brought about the combination may have been in operation since the creation of man. The production of any epidemic disease is not due to atmospheric influences alone, nor to the morbific influences of terrestrial emanations alone, but to the combined influence of both, and the existing constitution of the individual; all thus forming a combination of circumstances always changing, and always differing from those immediately preceding.

In this manner we account for the changes which the same diseases have at various times presented in their forms; and while species of human maladies, altogether new, such as small-pox, measles, and hooping-cough, add to the nosology of medical science, diseases that formerly existed altogether disappear.

In the particular "*combination of circumstances*" we are also to find an explanation, why every one exposed to any contagion does not become affected with the disease.

In every individual those conditions which I have mentioned for the development of the disease do not exist; the relation of the individual's constitution to the surrounding elements still enabling him to resist morbific influence, such as that of contagion, or of miasmata.

The particular change in the system to which, therefore, I would ascribe the occurrence of local exudation, appears most probably to consist in a vitiated condition of the blood, from the presence of some morbid matter, or from an excess of some natural constituent. Why an exudation depending upon such a general cause should locate itself in one organ rather than in another, is a question still undetermined. The most rational explanation appears to me to bear some relation to the fact, that increased activity of function in an organ renders it more liable to exudations from the blood-vessels into its substance. The anatomical constitution of an organ also modifies, in some degree, any exudation into its texture, the tissues of which it is composed having some affinity for the morbid material in the blood, or the natural ingredient which is in excess. M. Rayer, in noticing the morbid appearances of

typhus in animals, has related, that in the horse and the ass, the patches of Peyer in the intestines are the frequent seat of an exudation from the blood-vessels under typhoid conditions of the system ;* and it is also worthy of notice, that Peyer's glands in the *herbivora* are comparatively large. In warm climates we know that the activity of function in the liver is increased ; and we also know that in warm climates the liver is the most frequent seat of exudation from the blood-vessels. In females in whom unusual activity of the generative organs exists, the uterus is frequently found to be the seat of disease ; and in circumstances where the functional activity of the lung is increased, we are likely to have exudations of *liquor sanguinis* into its substance.†

The particular form of organization which the deposit assumes, and the degree of perfection to which it attains, are also to be referred, in a great measure, to such a systemic agency as a diseased condition of the blood ; and these characters will also be seen to depend more upon the nature of the constitutional evil, than upon the particular stage at which the deposit is examined. This feature will be more particularly brought out, when we contrast the pulmonary exudations in the various conditions of disease. Thus the exudations during the progress of Bright's disease, typhus fever, tuberculosis, or carcinoma, differ in respect of the amount of organization from each other, although the differences are not always so well marked as to enable us to determine, by microscopic examination merely, that any given specimen is characteristic of typhous, tubercular, or carcinomatous deposit, or exudation during Bright's disease, without also taking into consideration the circumstances under which the deposit occurred. The explanation we have now given of the general cause of the exudation we shall find to be consistent with the recorded facts of the individual cases, and also with the relative appearances presented by a minute examination of the exuded products.

I therefore look upon the morbid condition of the blood as the cause of *three* effects :—

1. Of the fever or constitutional symptoms which accompany or precede the effusion.
2. Of the exudations from the blood-vessels of the *liquor sanguinis*.
3. Of the *form and perfection of organization* which the exuded products attains.

I shall now proceed to consider the forms under which exudations from the blood-vessels of the lungs become organized.

When the first local lesion has occurred, namely, the rupture

* Lancet, vol. ii. 1842-43, page 373.

† In animals fattening in stalls, such activity of the respiratory function is required for the proper deposition of fat, and cattle are very liable to exudation into the substance of the lungs.

of the capillaries, accounting for the presence of blood-globules in the expectoration, as well as in the products of exudation, the more characteristic, appreciable, and unmistakable changes take place in the diseased part itself, and in its secretion. The tendency of the deposit is to pass into organisms of a particular form, —organisms depending for their characteristic appearances,—

1. On the nature of the morbid condition of the blood.
2. On the amount of vascularity which the affected part retains.

In other words, the characters of the new formations will be found to vary with the *quantity* and *quality* of the blood; and I am also inclined to ascribe much more influence to these two circumstances in modifying the appearances of the exudation, than I am willing to allow to the power of affinity exercised between the histological elements of the structure in which the exudation takes place, and the constituents, normal or anormal, of the blood.

When the first change in the deposit takes place, the functions of the capillary vessels are not suspended; circulation, although impeded, still goes on in the part; and while effusion of blood plasma, and extravasations of blood itself, are insinuated into every minute space, imparting a degree of solidity to the texture, a great portion of the serum is at the same time rapidly absorbed. The quantity of red blood-globules extravasated with the liquor sanguinis varies with the amount of rupture which has taken place in the capillary vessels, and on this circumstance does the redness of the exuded matter depend, as well as on the increased amount of capillary injection. "By this change the lung at first sight would seem to acquire increased hardness, and in point of fact it becomes more dense, and rapidly sinks in water. Reflection, however, will show that the term 'hardening' here is merely comparative. A lung so affected is undoubtedly harder and heavier than it was in its previously spongy, light, and healthy state, on account of the displacement of air by the solidified exudation. But if the finger be thrust into a healthy, and then into a hepatized lung, it will be found, that whilst the former offers considerable resistance, the latter is friable, and readily breaks down, proving that in point of fact a softening of the tissue has taken place."* According to authors, the specific gravity is increased as compared with the healthy lung in the proportion of 1·15 or 1·19 to 1, and the condensation throughout is generally complete, without a vestige of crepitation. The cut surface appears uniformly studded with flat granular elevations which are easily effaced. The pathology of this granulated appearance is differently accounted for by authors on pneumonia. Laennec considered the granulations to be the air-cells converted into solid grains by the thickening of

* Bennett, Treatise on Inflammation, page 35. Hence Andral speaks of hepatized lung as *softened*.

their parietes, and the obliteration of their cavities by a concrete fluid.* Andral considered that pneumonia essentially consists in an inflammation of the pulmonary vesicles, the internal surface of which secretes a liquid, at first muco-sanguineous and then purulent. In proportion as the inflammation advances, the liquid secreted becomes more thick and viscid, until at length it cannot be expelled from the cavity, where it is lodged and first formed. Accordingly it accumulates there, obstructs and distends the air-vesicle, and gives origin to the numerous granulations of which the tissue of the lung, in red hepatization, appears specially formed.† Louis, judging from the appearances of an injected lung, has come to the same conclusion.‡ More recently, however, we find Andral changing the opinion he first entertained, and stating, that "the morbid alteration is produced by a considerable degree of sanguineous engorgement of the parietes of the capillary bronchia and air-vesicles, the effect of which is to diminish or obliterate their cavities."§ Such is also the opinion of Stokes.‖ Another view has been adopted by Williams, namely, that the "granulations consist of little bunches of air-vesicles, whose membranous tunics have been so swelled by the deposition of a soft albuminous matter in them, as well as from the increased size of their blood-vessels, that their cavities are obliterated."¶ Hasse** and Rokitansky†† adopt the view first held by Andral, namely, that the granulations result from the filling of the air-vesicles with effused matter. From the foregoing review of opinions, it appears fully evident that the air-vesicles, or the cincture of blood-vessels surrounding them, may give rise to the appearances in question, from particular morbid changes occurring in these structures. It remains to be shown what these morbid conditions are. Is it an infiltration of the air-vesicles with an exudation of liquor sanguinis from the vessels, or is it an accumulated secretion of epithelium in the cells? From my own observation, I am inclined to consider that a granulated appearance to the naked eye may be produced, either by an exudation of liquor sanguinis from the cincture of pulmonary and systemic capillaries surrounding the air-vesicles, penetrating the diaphanous membrane lining the air-cell, or pressing the membrane together without such rupture; or, the appearances may be produced by an accumulated secretion of epithelium without any exudation of liquor sanguinis into the vesicle. The granulated appearance may also be produced by a combination of all

* On Diseases of the Chest (Forbes' Trans.), p. 201.
† Clin. Medicale, t. iii. pp. 312, 313.
‡ Researches on Phthisis, Sydenham Soc. Ed.
§ Pathological Anatomy (Trans.), p. 512.
‖ A Treatise on the Diagnosis and Treatment of Diseases of the Chest, p. 312.
¶ Cyclop. of Prac. Medicine, t. iii. p. 410.
** Path. Anatomy (Sydenham Soc. Trans), p. 209.
†† Handbuch der Pathologischen Anatomie, iii. band, p. 90.

of these conditions. In no two instances is it likely to be caused by the same morbid change; and, according to the stage at which the exudation has arrived in forming the granulated appearance, epithelium, compound granular corpuscles, or pus, will be found to be its component parts. Dr Henderson has found the granulations to contain "blood-discs, granules, and globular bodies," which he considers to be the cells of the epithelium; and if reference shall now be made to Case 7, detailed at page 34 of this paper, it will be found that the granuations could be picked out entire, and that the contents consisted of pus-like corpuscles, compound granular cells (exudation cells), and blood-discs adhering together. Under a low power (from 10 to 25) they appeared like large glistening cells with fluid contents, on whose outer surface little vascular twigs ramified. In Case 3 the granulations were composed chiefly of pus (see page 24). The condition of a lung which is the seat of an exudation of blood-plasma, I shall now describe as seen through the microscope.

After coagulation of the fluid effusion has taken place to a greater or less extent, the first change seems to be the formation of granules in its substance, so that a section of the tissue obtained by the aid of Valentin's section knife exhibits the pulmonary textures enclosed in a coagulum, and displaying a number of blood-discs imbedded in a nearly amorphous, slightly granulated or striated mass. At first no cells exist other than oval or cylindrical epithelium and blood-globules; but soon the formation of distinctive cells takes place in the exuded matter, and these cells assume a form of organization, first described by Professor Gluge as peculiar to inflammatory products in any part. Describing the alterations of the blood in inflamed parts, he observes, "that the blood-globules lose their tegument and their colour (a fact noticed previously by Gendrin), their nuclei alone remain; these, however, do not remain solitary, but by means of a whitish connecting substance become agglomerated, and form dense, opaque, round groups, containing on an average from twenty to thirty of the smaller bodies, which, examined singly, are quite light and transparent. By means of pressure or acetic acid, the associated granules break down into the individual bodies, and we see that the opacity is merely owing to the association. The associated bodies have a diameter in the mass of from $\frac{1}{50}$ to $\frac{1}{30}$ of a millimetre; the single granules are from $\frac{1}{500}$ to $\frac{1}{400}$ of a millimetre. These associated bodies," says Gluge, "I have seen in the blood-vessels, so that we have not here to do with a fluid which, transuding through the coats of the blood-vessels, is changed into granules. They escape by bursting the capillaries."* The idea

* Anatomisch-mikroscopische untersuchungen zur Allgemeinen und Speciellen Pathologie. 1st Heft, p. 13.

entertained by Gluge, which I have now stated, regarding the formation of these bodies, does not accord with observation; and from the recent examination I have made of cases, in which the lungs were more or less involved by deposits in various stages of development, I shall describe, as far as I have seen, the conditions under which the corpuscles of Gluge are formed. (This is the "compound granular cell" or "exudation corpuscle" of Bennett and other pathologists.) That this cell or corpuscle is not formed within the blood-vessels, is apparent from an examination of the exudation of blood-plasma into many textures, and more particularly in the brain; for, first, the exuded matter coats the blood-vessels exterior to their walls; and, secondly, the formation of the corpuscle of Gluge can be traced through the following stages, as described by Vogel, Bennett, and Reinhart.

1. The formation of clear, transparent, non-nucleated cells may be observed.

2. The formation of cells with a nucleus and nucleolus are seen, differing from pus corpuscles in their large size (the 200th to the 100th of a line), and in having a single nucleus. These are formed in the fluid of coagulated exuded matter, and become gradually filled by minute granules, which, when few in number, readily admit of the nucleus being seen. Subsequently, however, they conceal it; and the originally smooth cell membrane becomes rugged, the granular cell appearing as a spherical agglomeration of granules. Subsequently the cell wall appears to vanish, the enclosed granules to separate from one another, and to fall into irregular heaps, and each individual granular cell to undergo, in a minute scale, the very same process which a mass of coagulated fibrin undergoes in its conversion into pus-corpuscles.*

As to the compound granular corpuscle thus described, I have found the following to be the general facts:—

1. They are formed in greatest abundance during the first stage of the exudation (the second stage of pneumonia, according to Laennec).

2. As long as the capillary circulation is going on, and before complete stagnation has taken place.

3. When the redness and condensation is the greatest, the corpuscles begin to disappear.

4. They disappear altogether as the red softening passes into grey.

5. They are imperfectly formed, or not at all, in the deposits that occur during the progress of typhus fever.

Other changes are also to be observed besides the formation of the compound granular cell in the deposits which take place in the lung. These changes are to be sought for in the simple textu-

* Vogel. Path. Anat. (trans.) p. 156.

ral elements of the part. The epithelium becomes enlarged in appearance. Originally, and in health, the epithelium cell lining the air-vesicles is of an oval form, but soon it decreases in size, becomes round, and loses its transparent appearance, or the cells become smaller, and of a more globular form. Two sources of change may thus be observed in the epithelium cells: (1) a change in the character of an individual cell; (2) a change of form depending on imperfect development, the cell being thrown off before it has arrived at maturity. The alterations perceived in the characters of the individual cells consists in their assuming a granulated aspect, approaching in form and appearance the compound granular cell. (Plate I. fig. 1.)

It has been conclusively shown by Reinhart, that the epithelium cells are sometimes transformed into compound granular cells, but that they do not always arise from such a source is proved by their great frequency in cerebral softening, where such an explanation cannot altogether apply to their formation.*

The change in the form of the epithelium depending upon imperfect development is well seen in the cylindrical form of the scale. In place of being a fully-formed cylinder, it is much diminished in size, of an oblong globular form, and very often non-nucleated. When we examine the sputum of patients, in whom the pulmonary substance is the seat of exudation, we may discover the changes I have indicated as taking place in the epithelium, independently of the existence of irritation in the larger bronchia. I have also frequently confirmed the observation of Dr Remak, made in the clinic of Dr Schönlein, namely, that branched bronchial coagula are almost always present, the altered forms of the epithelia constituting a part of their microscopic elements (compare and connect this statement with the fact I have recorded at page 3, about the lung in cattle). They appear to be composed of delicate filaments running parallel to the long diameter of the cylinder. Sometimes we have granular forms in the deposits, forming the chief part in their composition, closely adherent, and in some respects very much resembling the casts of the kidney tubes occasionally found in the urine of Bright's disease. The granules and granular cells very much resemble the compound granular cell. They are generally, however, more finely granulated, and resemble the altered form of epithelium, of which I have just spoken; and when associated with the apparently imperfectly-developed cylindrical epithelium, there is little doubt of that structure forming a chief part in the constitution of these coagula. Besides altered epithelium, however, the compound granular cell does sometimes form a part of the coagulum. In general, acetic

* Vinchow and Reinhart's Archiv. i. 1. 1847. Monthly Journal for February 1848.

acid dissolves the cell walls, and sets the granules free, leaving them undissolved; the filaments also are dissolved by this reagent, so that the whole mass is rendered transparent, obscured only by the granules.

Cases illustrative of the formation of the Compound Granular Cell.

Case 1.—Bright's disease—softening of corpus striatum—dysentery—exudation in left lung organized in the form of the compound granular cell.

Kenneth M'Lean, aged 45, admitted under the care of Dr Douglas, August 8, 1847, suffering from Bright's disease. He died on the 12th of November.

Dissection.—*Head.*—Considerable subarachnoid effusion at different parts of the cerebral hemispheres. A portion of the right corpus striatum a little softened, rest of the cerebral substance apparently healthy. A microscopic examination of the softened portion of the corpus striatum showed the blood-vessels intensely injected, with extravasated blood around them, and the exudation of liquor sanguinis organized in the form of compound granular cells, which, with loose granules, existed in great abundance. These cells were not acted upon by acetic acid.

Chest.—Left lung completely condensed in the upper part, extending throughout its posterior half. When cut into, it presented a dark-red surface, finely granular, and emitted very little fluid on being squeezed. The lower lobe was not condensed, and emitted a frothy fluid on being cut into. The right lung was condensed in its inferior lobe, similar to the upper lobe of the left. On the superior lobe the bronchia had their vessels much injected, presenting an appearance of abnormal vascularity, with a copious exudation of mucus. A microscopic examination of the condensed portion of the lung made upon a thin slice cut out by Valentin's double knife, showed that these parts were completely void of air, and that their microscopical elements consisted of compound granular corpuscles, fine granules, and small globules of fat, with blood discs in abundance. (Plate I. figs. 3 and 4.) The fibrous tissue of the lung was distinctly seen, the individual fibres being more or less irregularly separated from each other by the presence of the granules and the compound granular cells. The usual empty interspaces formed by the fasciculi of the pulmonary fibres were also filled by these organized forms of exudation, but the whole could be washed away, leaving the fibrous tissue of the lung completely intact. In every part examined, the quantity of blood was considerable, and generally coagulated within the vessels. The aortic valves of the heart were slightly incompetent, and on one there was a slight deposit. The aorta itself presented numerous miliary deposits.

Abdomen.—Liver small, but apparently healthy. Kidneys granular—external cortical substance whitish and increased in extent. Lower part of the colon thickened, and the mucous membrane extensively ulcerated.

Remarks.—In this case Bright's disease of the kidneys was undoubtedly the primary affection, and the most important one as bearing upon the existence of a dyscrasia in the blood. That exudation of *liquor sanguinis* existed in the lungs, the brain, and the intestines, we had physical signs and constitutional symptoms during life, confirmed by dissection. The occurrence of convulsions some days before death, was not a symptom sufficient of itself to create a suspicion that an exudation of *liquor sanguinis* was going on in the brain, causing the appearance of softening it presented after death; but when we connect their existence with the tendency during Bright's disease to the "inter-current inflammations," then our suspicions might justly be excited by the occurrence of convulsions. The stage of hyperæmia, and of the formation of compound granular cells along with separate granules, constituted the organized elements of the deposits in the lung, along with an increased development of fat. Of the formation of fat in the lung, increasing with the amount of disease in the pulmonary texture, I shall have occasion to speak more at large in a future part of this paper. At present, it is enough to connect the two facts together, namely, the complete absence of air in the condensed portions of the lung (indicating that in the condensed part the lung was not performing any of the functions of respiration, as far at least as the oxygenation of the blood was concerned), and the existence of fat in the condensed portion in abnormal abundance. I shall attempt to show, that suspension of the functions of respiration in the part is one condition for the development of fat in the lung. From the length of time which this man had suffered, it is evident that exudation of *liquor sanguinis* in the lung and its reabsorption had been pretty equally balanced; and it is one of those cases of Bright's disease which shows (as all the other cases which I have examined tend to show), that there is no deficiency of organization or tendency to imperfect development of cells in the *liquor sanguinis* exuded into the textures during the progress of Bright's disease. In consequence of the nature of the existing dyscrasia, the exuded products, in organs seeming to be characterised by activity and perfection of organization, as shown by the general abundance of the compound granular cell.

There is another condition of the lung deserving of special notice, before considering the disintegration of that form of exudation in which the compound granular corpuscle forms the chief element of organization. The condition to which I refer is one

in which the product of exudation assumes a fibrinous form, and becomes mingled with the pyoid corpuscles of Lebert, and sometimes with nucleated caudate cells. Under such circumstances the exuded matter is apparently more or less influenced by the nature of the texture in which it is effused; and, accordingly, a lung in which the exuded *liquor sanguinis* assumes such a form of organization presents appearances under the microscope which may be denominated *cirrhosis*. The fibrous meshes of the pulmonary tissue seem to be increased in thickness by the fibrinous material exuded becoming organized around the individual fibres. The cut surface of such a lung appears of a bluish tinge, somewhat fibrous, and accompanied by an increase in the consistence of the part which feels tough and resistent. Such a condition of the lung may either precede the formation of the compound granular cell in the exudation, or the *liquor sanguinis* may become organized in both these forms at the same time.

Case 2.—Pleuro-peripneumony.—Robert Gilmour, aged 13, admitted December 31, 1847, under the care of Dr Robertson, suffering from febrile symptoms of an inflammatory type. About a week after admission he complained of pain in lower part of left side, over the region of spleen, which seemed enlarged; till then no local pain existed. The whole left side of chest now became dull on percussion, the respiration harsh and bronchial, with expectoration of translucent tenacious sputa, sometimes tinged with blood. The cough increased, and the expectoration became more frothy and less viscid; so that, notwithstanding treatment, the oppression of respiration increased, friction could be heard on both sides, and he died eighteen days after admission.

Dissection.—*Chest.*—Pericardium distended, and containing about four ounces of darkish serum, in which floated numerous flocculi of lymph. Heart and valves healthy. Left pleura contained a large quantity of serous fluid. Its layers were partially adherent by an abundant deposit of a yellow colour and soft consistence. The adhesions to the diaphragm were firm. On the surface of the right pleura, over the lower lobe of the lung, there were a few small patches of recent lymph. The whole of the left lung, with the exception of the apex, was much condensed, and generally of a bluish-red colour, and in some parts so completely void of air as to sink in water. A section from the condensed portion, made by Valentin's double-bladed section knife, presented a granular or molecular aspect without reagents, interspersed by fibres, generally running in one direction, and sometimes crossed by the filamentous tissue of the lung enclosing the air vesicles. These air cells were thus generally obliterated, so that very few globules of air could be detected, and few compound granular corpuscles could be seen. Some large cells, how-

ever, containing granules and nuclei, were visible amongst the molecular and fibrinous material exuded, along with colourless cells (Plate I. fig. 6). The elements of the exuded matter presented the general appearance described by Lebert as pyoid corpuscles, enclosed amongst fibrinous matter, consisting of a semitransparent amorphous mass. The fasciculi of fibres composing the pulmonary tissue were well expressed, and appeared in abnormal abundance, evidently from the fibrinous substance exuded attaching itself side by side with the individual filaments. This was demonstrated by the addition of acetic acid, which clearing away the fibrinous matter, left the individual pulmonary fibres clearly distinguishable. No air was visible under the microscope, and generally the tissue was comparatively free from blood. In the fluid squeezed from the tissue, some pale nucleated and non-nucleated cells were visible, with very few compound granular corpuscles (Plate I. fig. 5). Between the root of the left lung and the pericardium, a circumscribed quantity of pus was contained, apparently enclosed in a reflected fold of the pleura. Right lung much congested; otherwise, under the microscope, its tissue appeared healthy.

Abdomen.—Liver appeared normal in size and structure. Between the lower aspect of its left lobe, the stomach, and the spleen, there existed a circumscribed abscess about the size of an orange, containing dirty-looking purulent fluid. This was found to communicate with a partially-softened mass the result of exudation, into the substance of the spleen, involving about one-fifth or one-sixth of the whole organ, the rest of which was soft. The mucous membrane of the stomach was swollen, and thrown into protuberances on the posterior surface of the viscus by œdema of the tissue underneath. Other organs healthy.

Remarks.—The extent of the local lesions displayed by this case after death,—accompanied and preceded during life by febrile symptoms, much constitutional irritation, and physical signs of disease,—abundantly testify to the existence of a dyscrasia in the blood—a dyscrasia such as inflammation excited by cold or injury may produce in a system previously quite healthy. In the lung, the exuded matter assumes an organized form of so perfect a kind, that I am inclined to add another modifying cause to the existing dyscrasia, whatever that may be, for the influence of tissue is apparent in this case, causing the exudation of the *liquor sanguinis* to assume a fibrinous form, so as to associate its elements with the filamentous texture of the lung itself.

From these observations, it is evident that the exudation of *liquor sanguinis* into the substance of the lung may become organized in all the forms I have now indicated; that the combination of all these elements, namely, an effusion of the colouring matter of the blood and of the blood-globules, along with the

liquor sanguinis, passing into a more or less granular or fibrinous form, constitutes the second stage or degree of pneumonia, the red hepatization of authors, or the "*ramollissement rouge*" of the French. That these elements are susceptible of re-absorption, so that the lung may return to its normal condition, is still a problem unsolved. If this does not take place more serious changes follow. The immediate effect of the granular form of the exuded matter must be to compress the surrounding parts; and so long as exudation continues and is organized in that elementary form, a more complete stasis of the blood in the capillary vessels takes place; there is incomplete re-absorption and incomplete restoration of permeability to the pulmonary air-vesicles and capillary vessels; there is produced not only a local interruption to the circulation, but there is an impossibility of part of the blood undergoing the important change in the lungs of oxygenation, decarbonization, and the exhalation of moisture. The exuded material accordingly changes its nature and becomes purulent;* the formation of compound granular cells ceases to take place; those already existing become disintegrated; the blood-corpuscles extravasated with the exuded fluid undergo changes by which the globules become spherical, swollen, and at last break up; the whole mass assumes a more fluid form, and becomes entirely converted into pus. The changes undergone by the blood-corpuscle, when the exuded matter with which it is extravasated becomes purulent, differ from those changes which the blood-globules undergo when the condition of gangrene is about to be induced, and which I shall notice afterwards.

These observations also show that, with the condition of red softening, the greatest amount of constitutional disturbance exists, when much of the texture of the lung is implicated. The effects of impeded respiration and impaired sanguification become conspicuous, so that the existing dyscrasia (whatever that may be) is increased by the non-arterialization of the blood which passes from the lungs in a venous state into the general circulation. When this condition is established, the functions of the brain become disturbed, and, in many instances, death takes place by coma. The dyscrasia becomes also more apparent in the sallow complexion and almost icteroid condition of the general surface.

The elmentary organization of the exuded *liquor sanguinis* in the form of pus-corpuscles, and the disintegration of the compound granular cell, constituting softening of the pulmonary substance by the infiltration of its tissues with granules and pus, now deserve special consideration. The circumstances under which the exuded fluid assumes the elementary forms of pus are also those which are conducive to the development of fat in the affected portion of

* Lebert, Physio-Pathologique, vol. i. p. 128.

the lung. Accordingly, the amount of fat in the lung accumulates from the period at which the compound granular cells begin to disintegrate, onwards to complete disintegration of the tissue of the lung itself; and this accumulation takes place independently of the contents of the compound granular cell being composed of fat granules. During fœtal life the fat contained in the lungs amounts to 10·18 per cent.; but, after respiration is established, the proportion of fat in the normal condition of the lung never rises to above 6 per cent.* When, however, a portion of lung is rendered impervious to air by disease, the fat accumulates, and becomes, in relation to the whole weight of the lungs, 15·40 or even 50 per cent., according to the amount of pulmonary tissue involved. In this way the amount of fat in the lungs becomes relatively as great as the amount of fat in the liver, which always contains a large proportion. In the normal state, fat is now ascertained to exist in small quantity only as an essential constituent of the nervous tissue, as in the nerves and brain;† and it is only under the following conditions that fat accumulates in the textures of the body. If reference be made to the atomic constitution of fat, as compared with the ingesta and egesta of animals, it shall be found that in every tissue the formation or deposition of fat stands in a definite relation to the respiratory process, depending on the conversion of the carbon of the substances destined for respiration into carbonic acid by combination with oxygen. The abnormal condition, therefore, which causes the deposition of fat in any tissue of the animal body, depends on a disproportion between the quantity of carbon and hydrogen in the food, and that of oxygen absorbed by the skin or lungs, the oxygen being deficient. In individuals possessing an abnormal tendency to fatness, the circulation is out of proportion with the digestion; and such persons have in general very small lungs.‡ And, again, when the lung is diminished for the function of respiration, by any part of its substance becoming the seat of an exuded product, then that part is brought into circumstances analogous to any other tissue of the body, and subject to the same laws in regard to the deposition of fat. The production of fat is always a consequence of a deficient supply of oxygen, for oxygen is absolutely indispensable for the dissipation of the excess of carbon and hydrogen in the food; but the volume of air in which respiration goes on does not, under the influence of vegetable and animal life, undergo any change; and as the quantity of fat in the tissues increases when the oxygen absorbed by the lungs and skin in a given time does not suffice to convert into carbonic acid and water the elements of the non-

* M. Natalis Guillot, in Gazette Medicale de Paris, No. 29, 1847.
† Liebig's Animal Chemistry, 3d ed., p. 94.
‡ Liebig, loc. cit.

nitrogenized constituents of the food, the condition of the lung itself must be considered, when exuded fluid into its substanec has diminished its volume, as explaining the deposition of fat in its own diseased structure. A certain quantity of fat requires for its conversion into carbonic acid and water a certain quantity of oxygen; if this is withheld (as it always is to a greater or less extent in the part where exudation of *liquor sanguinis* has taken place) the fat is not consumed, but accumulates, for the blood conveys to the seat of disease the elements of fat in the form of carbon and hydrogen, with little oxygen; and these elements not meeting with more oxygen, are not dissipated in the form of carbonic acid and water, but are deposited in cells in the form of fat. If the lung, therefore, is to be looked upon as a structure destined for the elimination of fat from the system, the accumulation of fat in its texture during disease is to be regarded in the same relation as the non-elimination of urea in disease of the kidney, or the accumulation of any other product in the system which ought to have been eliminated according to the usual course of organic changes. During fevers, more especially typhus, the amount of emaciation, and consequent consumption of fat, must show, that if respiration is not performed by all parts of the lung alike, the elements of fat will not be consumed in those parts where respiration does not go on, but will be deposited as cells of fat, to be again absorbed and carried to those parts of the lung where respiration goes on, so long as life continues; or to those parts of the systemic capillaries where the formation of the carbonic acid and water, thrown off at the lungs, takes place. Of the accumulation of fat in the lungs under the circumstances I have now attempted to describe, I shall be able to offer abundant illustration in the cases that are to follow.

Regarding the formation of pus in the exuded *liquor sanguinis*, it is not yet clearly ascertained whether or not it is an independent organism. According to Vogel, it may be formed either from the matter exuded rendered solid, or from fluid exudation of *liquor sanguinis* before coagulation.* Pus has also been supposed to arise from the breaking up of the compound granular corpusele. In the *liquor sanguinis* exuded into the lung, it is apparent in most of our cases that the elementary forms of compound granular cells and pus-corpuseles exist together; and that, independently of microscopical observation, it has been an opinion generally entertained, that the several stages of a pneumonia are always developed out of the stage immediately preceding, and that the change always commences in the centre of the diseased part. However various, therefore, may be the opinions entertained concerning

* Vogel, Path. Anat., p. 144, trans.

the organization of pus in the exuded *liquor sanguinis*, there are only two possible conditions in which it can be supposed to occur.

1. It must either be an independent organism arising primarily in the exuded *liquor sanguinis*: or,
2. It must result from degeneration of the compound granular cell or blood disc.

If, however, it is found to possess an independent existence, the circumstances in which it is generated are also those in which the compound granular cell tends to become disintegrated, a fact which leads us to conclude that, although it may possess an independent existence, yet it may be called into being by the breaking up of the compound granular cell, which had enclosed in its structure the nuclei of the purulent formation. Hence, while the whole of the exuded matter assumes the form of granular cells or granular masses, the purulent formation finds existence amongst the debris of their destruction, although they may be independent and elementary forms of organization. In the purulent form of organization which the exuded fluid may assume, there is first of all observed a bloodless appearance of the texture, and if blood be at all visible in an unchanged state, it is always coagulated within the vessels. In general, however, all trace of vascularity is gone, and a section of the lung where this form of organization has taken place in the exuded *liquor sanguinis*, is characterized by a colour varying from dirty-grey or light-yellow to a melanotic tint; the shades of colour depending on the amount of vascularity, the amount of pigment whether normally present or the result of disease, and, lastly, on the changes which may have taken place in extravasated blood. A section being made through the exuded matter, the divided surfaces become immediately floated over by the purulent fluid, which appears uniformly infiltrated throughout the pulmonary tissues, filling up the air-vesicles, and separating the fibres, which, by washing with water or acetic acid, may be rendered free and generally distinct.

There is still another condition of the lung connected with a granular appearance on section, which has sometimes been looked upon as a form of grey hepatization; but as it is not the result of the organization of exuded *liquor sanguinis*, but of an excessive secretion of epithelium,* I shall only speak of it in passing, and attempt to notice its occurrence modifying the appearance of the purulent organization in any of the cases I have to relate.

Cases illustrating the organization of the exuded liquor sanguinis in the form of pus, and the development of fat in the seat of lesion.

Case 3.—Owen Hastings, aged 36, admitted under the care

* Henderson on the Anatomy of Pneumonia, Cormack's Journal, vol. i. p. 717.

of Dr Andrew, December 14, 1847. He underwent a severe attack of typhus fever, and his convalescence, although protracted, appeared to be going on favourably until the 2d of January 1848, when he complained of pain in the limbs, more especially the right, extending downwards from the knees, and attended with stiffness of the joints. There was no swelling of either limb, but the cuticle appeared to desquamate by small scales. On the anterior aspect of the right foot and leg there were some irregular patches of lividity. Three of the toes became almost quite black, their cuticle was hard and void of sensation throughout their distal phalanges; towards the roots of the toes the cuticle was slightly elevated. Immediately over the anterior aspect of the right ankle-joint there appeared some slight superficial ulceration about the size of a penny-piece, as if the result of a violent abrasion. No discharge proceeded from its surface, but the part appeared dry, hard, and scaly. By the 15th of January the swelling had extended to the knee-joint, and a sanious fetid discharge exuded from the ulcerated surface round the ankle-joint and the root of the little toe. On the 22d of January he had a violent rigor after leaving the bath, followed by increased heat of surface, and general vascular excitement followed by delirium. The right arm soon after became stiff at the elbow-joint, swollen, and painful. The pulsation in the right femoral artery was indistinct and small when compared with the left, and could scarcely be felt in the popliteal. For four days the condition of the arm became more painful; streaks of a purple hue stretched like cords along the inner aspect of the limb, which became highly œdematous. The circulation generally, both in the arm and leg, was languid, and the capillary circulation in the skin both of arm and leg was exceedingly feeble, as indicated by the length of time which any part took to regain its redness after being pressed upon. By the 30th of January, two of the toes of the left foot became discoloured at the distal extremity of their plantar aspect, and a red blush extended up the leg from the blackened part. An abscess formed on the ball of the great toe of the right foot, which opened and sloughed. An opening was made in the right arm, from which a quantity of fetid pus was discharged. The night before his death he suffered a severe rigor, followed by much dyspnœa and pain of chest. The whole right back became dull on percussion, and the lower part of the chest anteriorly; some crepitation could be heard in the infraspinous fossa of the scapula, and also in front below the nipple of the right side. He died on the evening of the 8th February.

Dissection.—*External appearances.*—Considerable emaciation; scaly appearance of skin on extremities; sloughy gangrenous condition of the toes of right foot.

Chest.—Slight and recent adhesions between the pulmonary and costal pleuræ of right side. About a pint of exuded fluid existed within the pleural cavity of that side, of a greenish hue, turbid with flakes of lymph in a semi-fluid state. The left side free from adhesions. The right lung throughout its lower lobe was condensed, easily broken up, and on section presented a yellowish-grey colour. The cut surfaces were rapidly floated over by a fluid resembling pus,—a microscopic examination of which showed fat granules and globules in considerable abundance, also pus-corpuscles, and a very few compound granular cells. A Valentin section from the grey hepatized portion exhibited no compound granular corpuscles, but the whole tissue appeared infiltrated with pus-corpuscles and small nucleated cells (Plate II. fig. 2). So completely did the exuded material infiltrate the tissue, that the mass was almost opaque, and no trace of air vesicles could be distinguished. Acetic acid brought into view vestiges of the filamentous arrangement round the pulmonary vesicles, and exhibited the nuclei of the pus-corpuscles. The meshes also of the pulmonary tissue, before obscure, were now made distinct, and, although much separated by the infiltrated fluid exuded from the vessels, were individually entire, and by no means broken down (Plate II. fig. 3). No compound granular corpuscles existed in these sections, and no cells other than pus and globules of fat soluble in ether. In the fluid taken from a portion of the lung where the purulent form of the exuded matter appeared to be commencing, a few compound granular corpuscles could be distinguished. Blood-discs also appeared in coagulated masses, and clear colourless cells were intermingled with pus-corpuscles of the usual form. Some of these pus-corpuscles were surrounded by a pellucid wall, apparently containing fluid, amongst which the pus-corpuscles could be seen to float, moving from side to side of the cell (Plate I. fig. 8). A considerable amount of congestion existed around the grey portion, as seen by a section, but no trace of the pulmonary vesicles were observed. The fibres were irregularly arranged, and the compound granular cells were few; and in proportion as a section was taken more and more removed from the purulent form of the exuded matter, the compound granular corpuscles increased in abundance and assumed a more perfect form (Plate II. fig. 4).

Surrounding the grey portion, and gradually passing from the grey colour to the red, the texture of the lung was friable, and from it a frothy fluid could be squeezed. The redder portion was not quite void of air, but of a granular appearance on section, which appeared to be the points of organization of the exuded fluid into pus as shown by the microscope (Plate II. fig. 1). The rest of the lung was much congested. The left lung, although somewhat congested, appeared otherwise healthy. The heart was firm in texture, and healthy.

Condition of the arterial trunks.—A large, soft, dark-coloured coagulum of blood, about a foot and a-half long, partially decolorised, was withdrawn from the aorta. Microscopically, it presented the appearance of coagulated fibrin, the striæ being mingled with blood-corpuscles and colourless discs about the size of the blood-globule. The artery of the right leg was laid open from Poupart's ligament downwards. In it a coagulum of blood existed throughout, varying in thickness as the calibre of the vessel varied. The same appearances were observed in the common iliac of the left side. On the right side the coagulum ceased to exist about two inches above the site of the ulceration, on the anterior aspect of the foot, where the anterior tibial artery was found contracted, indurated, and adherent to the *venæ comites*. The exuded matter completely obstructed the canal of the vessel, rendering it quite impervious. It presented granular matter, granules of fat, and crystalline structures under the microscope (Plate I. fig. 9).

Abdomen.—Viscera healthy, except right kidney, which presented appearances of fatty degeneration.

Remarks.—From the records of this case, it appears that typhus fever was the first condition of disease, and that all the other pathological changes followed in the chain of events connected with, and in some degree dependent upon, the condition which preceded any particular state. The course of the typhus fever was characterized by the grave nature of its symptoms, both of excitement and of depression, although during its whole progress it was unmarked by any symptom of local complication. It was not until convalescence was advancing (about the twenty-sixth or twenty-seventh day), and when the constitution seemed recovering from the first effect of the dyscrasia, that the vascular system showed symptoms, local as well as constitutional, that the coats of the arteries were the seat of some change; and the fact of exudation having taken place in the anterior tibial artery was demonstrated after death. That the capillary system seemed to participate in the disordered condition of the vessels is shown by the exuded *liquor sanguinis*, which, in the subcutaneous tissue of the arm, became organized in the purulent form, and which in the toes went on to gangrene; as well as by the scaly desquamation of the cuticle over all the parts contiguous to the more immediate seats of exudation. To a participation in this changed condition of the vessels, and also of the blood they circulated, I am inclined to attribute the exudation in the lung; and the relation subsisting between the changes in the blood-vessels themselves, and the purulent forms of the exuded fluid into the several parts, connect all these conditions as the sequelæ of typhus fever, which, although it had run its course, the coats of the vessels had suffered from the

existing dyscrasia. It may be somewhat more difficult to account for the exuded material in the lung assuming at once the state of purulent organization. If we look, however, to the great amount of substance involved, which, in a few hours, became at once condensed by an exudation so abundant, as by its pressure to preclude the possibility of blood circulating through the parts, we observe that its vascularity became entirely obliterated, absorption of any portion of the exuded fluid was rendered impossible, the essential conditions for the development of the compound granular cell did not exist, so that in a few hours the exuded *liquor sanguinis* became at once organized in the elementary form of pus; or it may be accounted for it in another way, as suggested to me by Dr Alison, namely, that the inflammation producing the exudation in the lung assuming the erysipelatous character as well as that on the surface of the body, tended to promote to fluid or purulent, not to *plastic* effusion, and therefore not to the formation of compound granular cells. The suddenness of the exudation, however, the abundance of the material exuded, and its fluid condition (maintained in that state by the abeyance of absorption), all exercise an influence upon the forms of organization.

Case 4.—Edward Grahame, aged 20, admitted under the care of Dr Douglas, February 29, 1848, had been in bad health for some time, on account of which he had taken mercury in such quantities as to cause ulceration of the fauces and gums. His symptoms, constitutional as well as local, indicated a diseased condition of the kidneys and lungs. He died eight days after admission.

Dissection.—*Chest.*—Heart and pericardium healthy. Lungs on both sides were much congested. The whole lower lobe and part of the upper lobe of the left lung was condensed, void of air, of a yellowish-red colour, and friable consistence. It sunk in water, and on pressure, an oily, purulent looking fluid flowed over its cut surface. Microscopic observation showed that this fluid was composed chiefly of pus-corpuscles. It felt sticky when pressed between the fingers, and considerable turbidity was produced by the addition of acetic acid. From these phenomena it appeared that mucus or epithelium cells also formed no inconsiderable portion of the fluid. Accordingly, under the microscope, along with the pus, various forms of epithelium were seen apparently thrown off from the basement membrane before they had reached maturity (Plate III. fig. 4). Round forms of epithelium resembling pus were also seen, but acetic acid did not dissolve any part of the cell, as it did to the pus-corpuscles, and at the same time set their nuclei free. Granules of fat and globules of oil existed in abundance, soluble in ether, among which were also to be seen little forms resem-

bling the "vibrions" described by Lebert* (Plate III. fig. 6), or they might be cilia shed from epithelium. This is the only time I have seen such an appearance, and therefore opinions ought to be suspended till more frequent observation shall furnish data. A Valentin section showed the air-cells completely disorganized and filled up by exuded material, the fibrous tissue by which they were surrounded irregularly distributed, so that the individual fibres were separated from each other by the infiltration of the exuded fluid and epithelium, as also of oil globules and fat granules. No compound granular corpuscles existed, and few blood discs could be seen (Plate III. fig. 5). Those which did exist were swollen, and apparently undergoing a change. No vascularity nor injection of vessels could be seen in the condensed portion, although these appearances prevailed around the seat of lesion. Acetic acid and washing with water rendered the texture of the lung distinct, and showed that the fibrous tissue was not broken down.

Abdomen.—In this cavity every organ and viscus appeared healthy except the kidney. Both were large, and had a considerable amount of granular deposit in their cortical substances.

Remarks.—The condition of the lung in this case shows, that the organization of the exuded matter in the form of compound granular cells cannot exist. How long exuded material had existed in its substance cannot with certainty be ascertained, the patient having lived only eight days after admission, and in such a condition as to preclude the hope of obtaining much information from himself. From the state of vascularity and injection in which the seat of lesion existed, it could only be expected that the exuded fluid would be organized in the form of pus. This state of vascularity could only be determined by the microscope, for the variety of colour in the healthy lung modifies its vascular appearance in disease. Accordingly, under the microscope no appearance of blood existed in the vessels, although, to the naked eye, the section of the lung was of a yellowish-red colour. The state of health in which this man appears to have been for some time previous to admission, and the treatment to which he appears to have subjected himself, is precisely one of those conditions of the constitution in which gangrene of the lung has been a frequent occurrence. Gangrene, however, had not commenced, as shown by the integrity of the pulmonary texture; and he appears to have died under the combined influence of cerebral oppression, *and the amount of texture involved* by the exuded material in the lung; both conditions being referable to the primary affection of the kidney. The appearance of vibrions (?) is another feature of interest. If such an appearance is really of the same nature as that described by Lebert, and

* Lebert: Physiologie Pathologique ou Recherches Cliniques, Experimentales et Microscopiques. Atlas, 1845.

which he found to exist in fresh pus from hospital gangrene, the condition of the lung, in the case I have related, is certainly ominous; and had life been prolonged, gangrene would in all likelihood have taken place, preceded by the generation of the parasites described.

From these cases, as well as from other observations, I may state shortly the conditions under which we may expect to find the exudation of *liquor sanguinis* in the lung becoming organized in the elementary form of pus. The conditions are,

1. A sudden exudation and abundance of exuded matter;
2. A great amount of tissue involved;
3. Diminished vascularity, and consequent
4. Abeyance of absorption, increasing the
5. Fluidity of the exuded fluid;
6. Breaking up of the compound granular cell, either liberating the nuclei of pus-corpuscles, or rendering the exuded material more fluid.
7. The stage at which the exuded matter is examined along with these conditions.

Having traced the organization of the exuded fluid through the most perfect forms of cell development, I come to consider it as terminating in a less perfect organization, depending on a specific dyscrasia of the blood, exercising a modifying influence over the forms which the exuded fluid assumes, as seen to the naked eye, and under the microscope in its more elementary parts. This dyscrasia is associated with the conditions of typhus fever, tuberculosis, and cancer. To the first of these conditions, namely, typhus fever, I propose to direct attention, as modifying the forms which exuded *liquor sanguinis* assumes during its progress, more particularly with reference to its condition in the lung.

A fluid condition of the blood is a characteristic feature in the morbid appearances of typhus fever; and there is reason to believe that such a condition also exists during life to a greater extent than in health, and that the exudations of its *liquor sanguinis* are but little plastic, of an unsightly dingy-grey, as if mixed with blood. The condition of the blood, however, varies with the stage of the fever, or rather perhaps the stage of the fever depends upon and varies with the state of the blood. During the first stage the blood is generally thick and dark, it coagulates rapidly, and forms a soft large dark-coloured clot. When examined at a more advanced period during the progress of the fever, it is found to be more fluid, of a scarlet colour; and latterly it becomes thin, watery, dark in hue, and ceases to coagulate. The following changes are also ascertained to take place in its constitution.

The watery portion of the blood increasing, the intensity of

the disease increases, and not merely are the solid constituents at that period diminished, but also the salts and carbonic acid. Stevens found the chlorate of sodium to be specially diminished, and the fibrin has also been found decreased in the blood of typhus fever, and it decreases as the disease advances. Hence deficiency in fibrin, in blood corpuscles, and in albumen, with the occasional formation of a salt of ammonia, may be looked upon as constituting the phenomena of a dyscrasia at once the cause of the fever, of the exudation of *liquor sanguinis* in any organ, and a modifying agent in its forms of organization. Under these circumstances it is maintained by many German pathologists, and more especially by Vogel and Rokitansky, that during the progress of typhus fever, "a certain morbid material, possessed of peculiar properties, and having a tendency to undergo certain metamorphoses, is poured out from the blood into the textures of organs and the tissues of parts." The local lesion seems to consist in an exudation of *liquor sanguinis*, in which are developed imperfect cells, molecules and granular matter. It has been attempted to assign to this deposit, occurring during the progress of typhus fever, certain specific characters supposed to be sufficient to distinguish it from other elementary forms of organization which take place in *liquor sanguinis*, organized under conditions of disease other than typhus fever. Of the examples of organized exuded matter, said to be that of the typhus deposit, which have been pointed out to me, a place might as readily have been assigned to them amongst *any* other defective elementary forms of organization, if *the circumstances under which the exudation occurred* had not also been taken into consideration. In tracing the nature and progress of any exuded product, the effects can only be examined as they are produced; and it is frequently not until these effects have existed for some time that we have any opportunity of examining them, and then we must, in every case, take into consideration the condition of disease (or departure from the standard of health) under which these effects were established. The parts most liable to become the seat of this (so-called) typhus material; or, in other words, the parts most liable to become the seat of exuded *liquor sanguinis*, which undergoes imperfect organization, are "the mucous membranes, especially that of the small intestines; but it is also admitted that the substance of organs, as of the lungs, may, during the progress of typhus fever, become infiltrated with a material closely resembling that found in the small intestines. The frequency with which the intestinal canal becomes the seat of extensive disorganization during the progress of typhus fever in Germany and in France, has afforded abundant opportunities for a close examination into the nature and cause of this disorganizing process; and the conclusions most generally arrived at by patho-

logists of these countries are, that this morbid process is attributable to the deposition of, and subsequent metamorphoses undergone by a peculiar product, which they denominate "the typhous material." In this country the intestinal lesion has occasionally occurred; and although its occurrence may be rare, yet the exudation of *liquor sanguinis* into the substance of the lung, characterised by imperfect organization and the deposition of fat in abnormal abundance, has been a most frequent and fatal complication of typhus fever; at all events, according to my own observation, it has been so in this city during the epidemics of 1846, 1847, and 1848. The commencement of the exudation was always insidious, and when discovered it seldom yielded to those therapeutic agents employed with advantage when exudation of *liquor sanguinis* had taken place under circumstances other than typhus.

"Of 63 cases of fever in the Edinburgh Infirmary, inspected after death, between March 1, 1846, and June 30, 1847, the spleen was the organ most frequently found affected; and next to the spleen, the lung was the most frequent seat of exudation. In 15 dissections it presented more or less consolidation from exuded matter, always differing in general appearances from the characters of hepatization in idiopathic pneumonia. It varied in colour, from a dirty-yellow tint to a brown-chocolate colour, existing frequently in masses of irregular but decided outline, varying in size, and resembling very much the deposit in the spleen."*

Of 101 cases of pulmonary lesion, inspected after death, between June 2, 1847, and March 13, 1848, 56 were the result of exudations occurring during the progress of fever, 34 of which were cases of undoubted typhus fever, in which 5 had intestinal as well as pulmonary lesion. It therefore appears, that during the present epidemic in Edinburgh, while an unusual number of cases of typhus fever existed, with the intestinal lesion so well described by Dr Waters, in his Inaugural Dissertation honoured by the gold medal of this University at the graduation of 1847; yet the present fever in Edinburgh has been especially characterised by pulmonary complication, as former epidemics in Edinburgh have been. In the intestines the products of exudation appeared in the solitary and Peyerian glands of the smaller viscera, in the follicles of the larger, and in the glands of the mesentery.

In the texture of the lung I purpose now to examine the organization of the exuded *liquor sanguinis* as modified by the existence of typhus.

In all the cases of typhus fever where an exudation of *liquor sanguinis* took place, the part existed for some time in the condition of hyperæmia, until the coats of the vessels giving way, every texture became surrounded by the liberated fluid, and ac-

* Bennett in Monthly Journal of Medical Science, p. 299. October, 1847.

cording to the existing dyscrasia, the form of organization was determined.

Rokitansky divides the progress of the local lesion into four stages, considered more especially with reference to the intestines.*

1. Exudation of *liquor sanguinis.*
2. A characteristic amount of organization, as modified by the existing dyscrasia.
3. Softening and disintegration of this deposit.
4. The result of this disintegration in partial death of the involved textures.

These phenomena are apparent in whatever organ the local lesion exists. In the lung are found various degrees of consolidation, according to the state of the blood, and the state of disintegration in which the deposit exists.

Generally, the organ or the part of it involved is of an unusually high specific gravity, but the texture is more friable, and rapidly the whole exuded material, and involved texture passes into a soft pultaceous mass. Its colour, when the process of disintegration has not commenced, is generally of a slate-grey or flesh colour; and when the deposit is well marked, it is limited by a vascular boundary, forming a line of separation between comparative health and local lesion, where all the vital changes take place connected with the loosening and disintegration of the mass. The exuded product never attains that degree of organization which it acquires when no such dyscrasia as typhus or tubercle exists. It takes place in the same manner, and holds the same relations to parts, as the exudation of *liquor sanguinis* under the conditions I have already considered. It fills the air-cells and interspaces, and undergoes changes in its organization depending upon the dyscrasia, as exuded products under other circumstances do. Its distinguishing feature is the imperfect power of organization which it displays. Round, irregular, and easily-dissolved cells are the highest forms of organization hitherto found in the deposits in the lung, always associated with numerous molecules and granules, which become more abundant as the process of softening advances. More frequently, however, molecular and granular matter, associated with particles of fat in unusual abundance, are all the morbid changes that can be detected; and when the lesion is at all extensive, or has existed for any length of time, fat is an invariable constituent; and generally the forms of the compound granular cell are entirely absent, the granular form of the exuded matter existing in masses without being enclosed in a cell wall. If the compound granular cell shall be considered as the highest form of organization which any exudation of

* Handbuch der Pathologischen Anatomie. Von Carl Rokitansky. III. Band, pp. 239, 240, 242.

liquor sanguinis can assume next to conversion into a texture analogous to another texture of the body, the imperfect and abortive attempt at organization in the material exuded during typhus fever is a feature whose constancy is worthy of observation. That the compound granular corpuscle is the highest form of organization, appears evident by reference to the conditions under which it occurs; and it is only in the early stage of typhus that such organizations appear. More frequenty, however, the exuded matter assumes the form of masses or clusters of granules; and as the disease advances, or when the products of exudation are examined at a later stage, then these granules have become still more diffused, mingled with small globules and granules of fat. This condition of the compound granular corpuscle, or rather of the granules which ought to compose it, affords a marked illustration of the power which the typhus dyscrasia exercises in modifying the organization of the exuded *liquor sanguinis*.

The period at which exudation seems to take place, or within which the typhus dyscrasia seems to exercise its greatest influence as a modifying agent, appears to be between the first and the tenth day; and when once the exudation takes place, it seldom recedes, accounting for the failure of the usual therapeutic agents, in modifying the symptoms, or in promoting resolution when the exudation is at all extensive. The diagnosis of exudation into the lung during the progress of typhus fever can only be made out with certainty by the stethoscope, constitutional symptoms being generally entirely absent or altogether obscured by the typhoid condition. The changes which the exuded matter undergoes are its conversion into imperfect cells (which cannot be recognised independently of their situation, and the circumstances under which they are formed), softening or disintegration of the exuded product, frequently accompanied with death of the texture of the lung itself. The cause of this imperfect organization I have already stated to be the morbid condition of the blood, as characterised by its deficiency in albumen and fibrin. The deficiency in albumen cannot be without its influence on the process of organization; and when we connect this deficiency with the facts which I have to record regarding temporary albuminuria occurring during the fever, still more importance may be attached to the influence of such a morbid condition of the blood.

Cases illustrating the modifying influence of the Typhoid State upon the organization of liquor sanguinis exuded into the substance of the lung.

Case 5.—Elizabeth Callender, aged 32, admitted August 3, 1847, under the care of Dr Robert Paterson. She was treated in one of the tents at that time pitched behind the hospital. She

suffered from an attack of relapsing fever followed by typhus, of which she died on the 15th of August.

Dissection—*Chest.*—Left pleuræ slightly adherent by matter of a yellow colour recently exuded, which was easily broken up. The inferior lobe of the lung presented two dirty-yellowish patches, the larger the size of a five-shilling piece, the smaller the size of a half-crown piece. On section, these were found to correspond with two depositions in the parenchyma of the lung very much resembling the deposits in the spleen described by Rokitansky as typhoid. A microscopic examination showed this deposit to consist of an exceedingly fine molecular matter, without any trace of cell formation, intermingled with granules of fat, which ether dissolved, and acetic acid rendered the whole more transparent. (Plate II. fig. 5.) No compound granular corpuscles could be seen, and few blood discs. The whole exuded material was intimately mingled with the pulmonary fibres, filling completely and obliterating the pulmonary vesicles. In the vascular boundary, which defined and separated these deposits from the pulmonary substance, the blood-vessels were irregularly and unequally filled with blood. Exudation granules and globules of fat also existed in abundance, along with some broken-down or imperfectly-developed cells. (Plate II. fig. 6.) The upper lobe of this lung was congested, but no exudation had taken place. It yielded, on pressure, a copious frothy fluid. The right pleura was adherent throughout by dense chronic adhesions. The lung itself was puckered in two places,—very deeply in the inferior and middle lobe, and very dense to the feel. On section, the puckering corresponded to a firm, fibrous, slate-coloured cicatrix of stellate shape, the parenchyma surrounding which was of considerable density, from an increase of fibrinous development. The heart was healthy, but felt soft and flabby.

Abdomen.—The spleen presented in its centre a deep stellate puckering, corresponding on section to a firm cicatrix. Externally, at the puckered part, it was adherent by old bands of lymph to the diaphragm and peritoneum. Other organs healthy.

Remarks.—From the history of this woman, previous to admission, it appeared pretty evident that she had suffered from the first attack of the relapsing fever; and that, during its relapse, when she came into the hospital, typhus became developed. Her non-exposure to contagion is improbable, considering that her occupation was that of a washerwoman amongst the lowest purlieus of the city.

In connecting the symptoms of local complication with the appearances found after death, it is evident that the exuded matter in the left lung is the only lesion to be associated with her last illness; and the two facts, namely, the previous existence of spotted fever, and the appearances of old adhesions between the spleen and dia-

phragm, and of old deposits and cicatrices in the spleen and right lung, are worthy of being connected. The deposit in the left lung is the exudation of *liquor sanguinis*, whose organization has been modified by the present existing typhus dyscrasia. It occurred during the progress of the fever, manifesting its presence by increased constitutional disturbance, as well as physical signs, between the sixteenth and twenty-first day. Its microscopic characters I have described as molecular, amorphous, and opaque, intermingled with fat, and in some parts with exudation granules; all which appearances I look upon as the effects of the modifying influence of the typhus dyscrasia. She reported that she had suffered from typhus three years ago; but it is more consistent to suppose that she suffered from the epidemic fever prevailing at that time, with the existence of which I am inclined to associate the deposits and cicatrices found in the spleen and right lung. The most frequent deposits in the spleen have been found associated with short fever or its previous existence, as dissection and inquiry have shown.

Case 6.—A child two years of age, who expired under typhus, had an exudation of *liquor sanguinis* into the parotid gland; and the exuded material which filled the right lung existed in masses, some of which had commenced to disintegate. Two or three of the masses were excavated by central cavities, which were empty and collapsed, very much resembling the excavations left by the sloughing of a solitary intestinal follicle after disintegration of the (so-called) "typhous matter." No compound granular corpuscles could be detected in the exuded products; and the air-cells seemed to be the chief seat of the exuded material, whose elementary forms of organization consisted in granules associated with abundance of fat. The bronchial glands were slightly enlarged.

Remarks.—In this case I had reason to believe that exudation into the bronchia was the condition which immediately preceded an extensive exudation into the air-cells themselves, expanding the pulmonary vesicles after the manner I have described.

Case 7.—Typhus;—exuded products into left lung, with destruction of its texture.

John Brennan, aged 23, admitted under the care of Dr Andrew, January 10, 1848, suffering from typhus fever, and reported to be eight or ten days ill. He died thirteen days after admission.

Dissection.—*Chest.*—Recent adhesions between the pulmonary and costal pleuræ of both sides. On the left side lymph had been recently exuded. Both lungs were much congested. The right lung was somewhat condensed in its lower lobe, and very friable. The left lung throughout its lower half was of an intensely red colour, and so friable as to break down under the finger with the utmost ease. Its surface was here and

there interspersed with exuded matter of a whitish appearance, which on section presented points varying in size from a pin head to a barleycorn. These products of exudation were soft, and exuded on pressure a whitish substance resembling pus. They only existed in the lower half of the lung of the left side. On section the cut surface soon became very red and pultaceous, so that the particles of exuded matter could easily be picked out, leaving a cup-shaped depression in the soft pulmonary substance. Observing them in their natural position when not opened into, they presented an opaque whitish aspect surrounded by a distinct vascular base, resembling the summit of a pustule just approaching maturity. When removed from the lung and viewed through a low power (10 to 20 diam.), they appeared like large glistening cells with fluid contents, on whose outer wall little vascular twigs ramified. (Plate III. fig. 9.) They had none of the raspberry appearance described by Dr Addison in Guy's Hospital Reports, Vol. I., 2d Series. Their contents seemed to consist chiefly of pus-corpuscles, granular products of exudation, and blood discs adhering together. (Plate III. fig. 8.) The pus-corpuscles were imperfectly organized, or might by some be considered as young and altered epithelium. These elementary constituents were associated with fat. At the base of the lower lobe, a patch about the size of a half-crown piece, of a dark grey colour, and surrounded by a dark purple circumference, appeared upon the pleura. A section through this patch showed a gangrenous cavity about the size of a walnut. The dark purple appearance extended through the lung, and surrounded the cavity, which contained a dirty-white granular matter, easily washed out, and seeming to consist of chalky like particles. A membrane was exposed lining the cavity, which was crossed by the fibrous tissue of the lung. This part exhaled a very fetid odour. The misroscopic appearances of the material from the gangrenous cavity exhibited oil globules, granules, pus-like cells, blood discs, and "exudation masses" or compound granular cells modified by the existing dyscrasia. (Plate II. fig. 7.) The fluid from the upper lobe of the left lung was composed chiefly of coagulated masses of blood, of nucleated and non-nucleated transparent cells, and of exudation cells modified by the existing dyscrasia. A Valentin section from the friable portion of the lung surrounding the cavity showed altered blood, whose hæmatin had coloured the surrounding parts, but the pulmonary fibres were unbroken except within the cavity. (Plate III. figs. 1 and 2.) The bronchial glands were much enlarged, varying in size from a bean to a small egg, and slightly melanotic. Heart flabby, with a decolorised clot in the right ventricle; blood otherwise fluid.

Abdomen.—Liver somewhat congested, spleen soft and small. Other organs healthy.

Remarks.—In connection with these last two cases, there are several points deserving of notice; namely, (1) a great amount of fatty matter deposited, more particularly in the last case—a condition we must connect with the long-continued dyspnœa, depending in part on the cerebral oppression, as well as on the obstruction offered to the oxygenation of the blood by the amount of tissue involved by the exuded *liquor sanguinis;* (2) the condition of the exuded matter, as shown by its resemblance to the typhoid ulcer; and, (3) the enlargement of the bronchial glands completes an analogy between this morbid condition of the lung and the state of the intestines and mesenteric glands when they become the seat of exudation during typhus fever.

I would also remark in passing, that enlargement of the bronchial glands is a morbid condition almost invariably connected with some morbid condition of the lung itself, and ought not to be considered a disease *per se.*

Another case whose particulars I am unable to record for want of room, presented all the appearances of imperfectly-organized products of exudation connected with the typhous dyscrasia, along with an abnormal amount of fatty matter. An interesting and unusual feature distinguished it from all the rest, which was temporary albuminuria, apparently connected with the presence of pus in the urine. The interesting question regarding the absorption of pus at once presents itself; for its presence in the urine did not depend upon renal disease, nor upon any discharge from the genito-urinary organs. Pus, however, had existed in the lungs, and from the pulmonary tissue its presence in the urine is to be accounted for.

The absorption of pus, it is ascertained, may take place in two ways;* (1) as real pus absorbed by the vascular system, a lesion taking place in the coats of the vessel; (2) by the pus-corpuscle undergoing changes, rendering it fit for absorption as well as for elimination by the excretory organs. By both of these ways may the presence of pus in the urine be accounted for. A passage is obtained for the corpuscle through the pulmonary veins, whence it finds its way to the left ventricle; from which, by the blood, during the eliminating action of the kidneys, it appears in the urine either as pus, or as the crystalline formation of its metamorphoses.

Suggested by this case, and in reference generally to the cases of typhus fever, connected or not with exudation into any organ, I have still another condition to notice, and to which I am inclined to attach some importance in reference to the influence it may possess upon the phenomena of the existing dyscrasia. I refer to the diminution of albumen in the blood, which may be

* Zimmermann on the Absorption of Blood and Pus. Medico-Chirurg. Review, 1844.

connected with the temporary albuminuria sometimes found to exist during the progress of typhus fever, as well as during exudations into organs such as in pneumonia.

Dr Finger of Prague has found albuminuria, independent of renal disease, to exist in 155 cases out of 600 of various acute diseases, and that, next to tuberculosis, the temporary albuminuria occurred most frequently during typhus fever; next to which, in the order of frequency, followed puerperal fever and pneumonia. That in those cases of typhus fever which proved fatal, the intestinal complication existed in most, and the pulmonary in the remaining. We also find his researches showing that the albumen appeared in the urine generally from the sixteenth to the twenty-fifth day, while the disease was on the increase or at its height. In those who recovered, it uniformly declined and disappeared during convalescence. In 9 out of 15 cases of pneumonia, it disappeared during recovery. In 6 who died, no disease of kidney could be detected. In 26 cases of typhus fever, in which extensive exudation had also taken place into the lungs, I examined the urine in each, and found temporary albuminuria to exist in 6; and the following table (see next page) shows the conditions of the urine and stage of the disease at which the albuminuria appeared.

Of these six cases three recovered and three died, but in all of them, with the exception of one, the albumen disappeared, and in none was there any evidence of renal disease. In all the cases the albumen appeared on an average about the sixteenth day of the fever, and about the sixth or seventh day after exudation had occurred in the lungs. The average density of the urine appears to have been about 1024 at the time of coagulability. The disappearance of the albumen appears always to have been followed by a more or less abundant crystalline deposit, when the average density diminished.

Dr Finger, from his observations, concludes that the presence of albumen in the urine, along with fibrinous or purulent products of exudation into any organ, is in consequence of these products of exudation becoming absorbed and eliminated again as albumen by the kidneys. There is some inconsistency, however, about such an explanation, when we find that the albumen is invariably present in the urine during the exudation, formation, or organization of the exuded matter, in whatever organ it may take place, and that, during the resolution of this exuded matter, the albumen is absent at the very time when the products of exudation are being absorbed into the current of the circulation, and associated with an abundant crystalline deposit in the urine. From my own observation, I am inclined to regard the existence of albumen in the urine unconnected with renal affection as a symptom or part of

TABLE I.

Sex.	Age.	Day of Typhus.	Day of Exudation.	Character of Expectoration.	Character of Urine.	Result and Remarks.
Fem.	21	12	6 or 8	Viscid, purulent, bloody.	Coagulable, not transparent. Acid, sp. gr. 1·028.	
		18	12or24		Not coagulable—dens. 1·026.	As convalescence advanced, amorphous urates and epithelium appeared. Cured.
Fem.	18	17	6 or 8	purulent.	Coagulable — amber colour—acid— pus in urine.	Died. No disease of kidney—pus in urine from the lungs by absorption.
Fem.	19	20	?		Coagulable — yellowish-red—acid — sp. gr. 1·026.	
		28			Not coagulable.	Erysipelas of scalp.
		32			Not coagulable — sp. gr. 1·011.	Abundant crystalline deposit. Died. No dissection.
Mal.	21	22	10		Coagulable—blood — sp. gr. 1·019.	
		26	14		Coagulable — density 1·028 alkaline—uric acid crystals.	
		33	21		Not coagulable.	Abundant crystalline deposit. Died. No examination permitted.
Fem.	27	12	6 or 8	Scanty.	Coagulable—not clear —sp. gr. 1.020.	
		24	18or20		Not coagulable.	Amorphous urates. Cured.
Fem.	21	15or16	9or10	Muco-purulent.	Coagulable—turbid—of a light gamboge-yellow--sp. gr. 1·015 neutral triple — phosphates.	
		24	18or19		Not coagulable—acid —sp. gr. 1·019.	Abundant crystalline deposit. Cured.

the constitutional disease. Its deposition by exudation into the pulmonary substance, for example, constituting, according to its elementary forms of organization, those conditions which in this paper I have attempted to describe ; its existence sometimes, along with an excessive elimination of urea in the urine during

typhus fever, constituting part of the phenomena in the typhous dyserasia. In short, its co-existence in the urine along with local products of exudation of various kinds, as well as during diseases where apparently no such exudation occurred, must lead us to conclude that the albuminuria is a part of the disease; and its disappearance during convalescence still more confirms such an opinion. It is known farther, that in every disease there is a greater or less alteration in the state of the secretions; and probably, if more extensive investigations were made into the nature of the various excreted materials during acute diseases, phenomena would probably be found compatible with those conditions of disease in which albumen is deficient in the blood, eliminated by those organs and textures where changes in the blood take place during the processes of secretion and nutrition, as in the glandular structures, where it might either constitute an organized product of exudation, as in the lungs, or be eliminated along with the proper fluid eliminated by the gland, as with the urine secreted by the kidney. It is true we do not find such a condition in every case, but neither do we find tubercles in every organ, although tuberculosis is undoubtedly a constitutional disease; neither do we find carcinoma in every organ, although a constitutional disease; neither do we find exudation of *liquor sanguinis* in every organ, nor always in any organ during typhus fever, although a dyserasia evidently exists. Temporary albuminuria therefore is the more likely in proportion to the duration and severity of the constitutional symptoms, the nature of the existing dyscrasia, the extent of local lesion (such as the amount of lung involved by exudation), as well as in the functional activity of those organs where the blood undergoes a change for the purposes of life.

All the cases I have recorded of typhus fever are characterized by one feature, namely, imperfect organization of the exuded *liquor sanguinis;* but, independent of this, I have not found in any case characteristic cells which could be called "genuine typhous deposit," according to the classification of Rokitansky. It is generally in the mesenteric glands that the most perfect and highest degree of organization in the cell is said to take place, constituting the "genuine typhous deposit of Rokitansky," and therefore it is, that from this very localization I would doubt the existence of specific characters in the cell. It is sufficient to know, that in all cases of undoubted typhus fever, in which any exudation takes place into the texture of organs, the exuded products are marked by the absence of the perfect compound granular cell, and of perfect pus, and always present imperfectly-organized forms, granular masses, molecular and fatty matter, characters sufficient of themselves to distinguish the products of such exudations

occurring during typhus fever from the usual forms of organization, as I have seen in Bright's disease, or in a pneumonia occurring in a healthy person, where we have the most perfectly organized forms existing.

Certain it is, therefore, as these cases abundantly testify, that the existence of typhus fever modifies the exudation of *liquor sanguinis* in whatever organ that exudation may take place.

The last form of organization I have to notice, as having observed the exudation of *liquor sanguinis* to assume in the lung, is one of rare occurrence, in the human species at least,—I mean the formation of cartilaginous masses. In the museum of our university, there is preserved and beautifully injected, the lung of a dog, extensively infiltrated by an exuded product of a cartilaginous nature, existing in large nodules, apparently surrounded by healthy pulmonary tissue. The dog had evidence of a dyscrasia existing, if we may judge from the nature of the exuded matter and from the universality of its existence in the bony skeleton itself. All the bones throughout every part of their surface were the seat of an exuded product, with the exception of those parts subject to friction, as at the joints, or where the action of muscle, aponeurosis, or tendon exercised a similar influence. This exuded material was apparently organized as bone beneath the periosteum, traversing the Haversian canals, and even appearing in the medullary canal itself, as seen by a longitudinal section of a long bone. The exuded products existed in the form of little granular masses and spiculæ or small papillæ.

Case 8.—January 8, 1848.—At the dissection of a female, aged 65, who died from the effects of gangrene of the left superior extremity, there was found in the left lung five hardened masses, varying in size from a small pea to a nodule the size of a filbert. The smallest of these masses appeared to be a tubercle. It was soft, of a yellowish-white colour, enclosing in its centre a darker speck. Under the microscope it appeared to consist of granules distinct from each other, a few corpuscles, generally of an irregular form, containing two or three of these granules as contents. Another mass appeared like a nodule of cartilage enclosed in a cyst, to which it was adherent by blood-vessels. It was vascular and cut-like cartilage, disclosing a small triangular cavity in its interior, containing about two drops of a glairy fluid, chiefly composed of blood-discs. The lining membrane of the cyst in contact with the nodule was lined by epithelium, and was highly vascular. It seemed to be surrounded by healthy pulmonary tissue, which was the case with all the masses, so that they appeared as if harmless foreign bodies; and if once tubercular, they had lost their malignant type. In this mass the microscope disclosed cartilage cells surrounded by

fibrous tissue. (Plate III. fig. 3.) These cells were not affected by acetic acid, and were easily put out of their relative position by the slightest pressure. Having made out the identity of this mass with cartilage, the question immediately suggests itself, namely, "how came cartilage there if tubercle once existed?" It is not improbable that cartilage presenting such an appearance in the mass at one time enclosed a tubercular cavity; for it has been found, and stated by Louis (Researches on Phthisis, page 9), "that when the disease is of long standing the membrane investing the cavity is dense, almost semitransparent, semicartilaginous, about a quarter of a line thick, and generally itself lined with a second membrane." It is therefore possible that such a cavity once existing in the case I have mentioned, may have contracted upon itself until it has assumed the shape, size, and general aspect described. A cartilaginous tumour developing itself in a gland is rare, and its mode of *epigenesis* is not yet explained. The most probable explanation of its *existence* is the one I have related, and the chances are in favour of the pre-existence of tubercle, since one of the little masses presented all the appearance of a tubercle, both microscopically and to the naked eye. The other cretaceous masses were not uniformly hard, but varied in consistence in different parts, and in some of the softer portions the characters of tubercle were apparent. The harder parts consisted of chalky particles quite amorphous, breaking down under pressure in water, rendering it turbid and white. In all the cretaceous masses numerous crystals of cholesterine were found, bearing testimony to the advanced age of the morbid product. The structure of the lung surrounding each of the masses, although healthy in general appearance, was much condensed in their immediate vicinity, with here and there a considerable quantity of spurious melanotic deposit (black pigmentary matter) arranged in irregular masses, and composed of a number of minute granules aggregated together. The great abundance of this deposit is another proof of the old formation of the masses. If we refer to the researches of Lebert on tuberculosis, we find that the most important element in the interior of a pulmonary ulcer is an organised *membrana pyogena*, intimately connected by minute blood-vessels with the subjacent pulmonic tissue, and presenting a reddish velvet-like vascular appearance. In the predominance of fibrous tissue, and the small degree of vascularity, this structure sometimes assumes a cartilaginous appearance. In this way I imagine the organization of the exuded matter has taken place in the case I have described, which seems to be a most perfect illustration of the healing of tubercle, both by calcareous transformation, as well as by the exudation and organization of *liquor sanguinis*, effecting cicatrization by contraction of the cavity.

Such are the forms of organization and the anatomical relations

which exuded *liquor sanguinis* may assume in any organ; and from the cases I have related, it must be apparent, that according to the morbid condition of the blood, so is the organization of the exuded material; and, that of all morbid conditions, typhus fever exercises the greatest modifying influence.

Hitherto I have considered the products of exudation in all its forms of organization, and find that for the most part they pass into temporary forms which do not involve the proper tissue of the lung either in their growth or their destruction. The only lesions of structure which exist in the substance of the lung itself are rupture of blood-vessels, and generally, also, solution of continuity in the lining membrane of the air-cells, with a separation of the individual fibres from one another in consequence of infiltration by the organized forms of the exuded matter. There is therefore no physical reason why these temporary forms originating in the products of exudation should not by their reabsorption leave the proper texture of the lung comparatively uninjured. It is not, therefore, the amount of texture destroyed in the lung which is the cause of death, but it is the amount of texture which, for the time being, is rendered unfit for the exercise of those functions essential to life, and which, if suspended for a time, necessarily cause death. The exuded matter, however, does sometimes display a tendency to become rapidly disintegrated, and to involve in its destruction the tissue of the lung itself. The breaking up into fragments, and disintegration of the filamentous tissue of the lung, constitutes the condition of "gangrene," in which every simple element of the texture becomes changed; neither blood, fibres, nor epithelium can be seen in their perfect form; and the whole mass is converted into an amorphous granular character, of a yellowish-brown or black colour, mingled with drops of fat. The tissue becomes soft and flaccid, in some parts perfectly liquescent, and emits a fetid smell. The texture becomes broken up, and shreds of fibrous tissue are here and there to be seen by the microscope along with the debris of textures in various forms. I shall not trespass upon the limits of the Journal by a recital of cases. Suffice it to say, that they present nothing which has not been already observed in cases of a similar kind. The rarity, invariable fatality, and apparently mysterious character of pulmonary gangrene, has obtained for it a melancholy interest wherever it has occurred; and, accordingly, since Laennec directed attention to its peculiar characters, pathologists of the greatest ability have contributed to the records of the disease. Notwithstanding the researches of Andral (1822), of Lorinser, of Schroeder Van der Kolk (1826), of Bright (1827), of Cruveilhier (1833), of Guislain (1836), and of Craigie (1841), it is still a condition at all times

difficult to diagnose, and its existence is often unknown until the disgusting appearances after death proclaim a condition which general symptoms during life failed to disclose, and hardly ever led to a suspicion. The diagnostic symptoms usually recorded are derived from the expression of the countenance becoming small, pinched, and contracted, haggard, ghastly, miserable, and death-like, eyes sunk and void of lustre, patient squeamish and languid, with occasional vomiting, and a feeling of indifference to all external objects, all of which symptoms may or may not be associated with a disgusting fetor of the breath, but which when present may be considered conclusive. Not one of all these symptoms, however, may manifest themselves, and yet the condition of gangrene may exist. From the recorded cases, therefore, as well as from the cases I have seen, it may be of some importance to classify the conditions of disease in which pulmonary gangrene has occurred, considering that the causes determining to gangrene of the lungs are still acknowledged to be unknown. The exudation of *liquor sanguinis*, terminating by gangrene of the lung, is by all authors considered as one of the least frequent terminations. Morgagni only records one case, and Laennec is reported to have seen only six or eight during the whole course of his practice. That exudation of *liquor sanguinis*, however, does sometimes terminate in gangrene, is clearly shown, both by constitutional symptoms and physical signs during life, confirmed by the state of the surrounding parts after death. The insidious and often sudden mode of its attack, the sudden, remarkable, and fatal collapse which supervenes, show at the same time that no local condition is suspected to account for the presence of gangrene. The extent to which the destruction takes place also varies much. In every case we have the formation of a slough, its liquefaction, and the establishment of a cavity. Sometimes we have nearly the whole of a lung going at once into gangrene. At other times we have only a small portion in the centre of exuded matter, as in Case 7, related at page 34. Sometimes we have a line of separation attempted to be formed; at other times we have no attempt made to limit the extent of the destruction; and this latter diffuse condition I have generally found associated with cases in which some dyscrasia existed as in typhus fever.

Of 15 cases recorded by Guislain—
All were maniacs.

Of 3 cases recorded by Van der Kolk—
1 was a maniac,
2 laboured under a peculiar condition of the body.

Of 6 cases recorded by Dr Craigie—
2 were mentally deranged with lesion in the brain,

2 suffered from Bright's disease and mercurialism,
1 had variola, and
1 had typhus.

Of 15 cases in our own hospital—
4 had typhus,
3 fever (type not noted),
4 suffered from ill health and mercurialism,
2 had tuberculosis,
1 suffered a blow,
1 had lesion in the brain.

These cases may be classified as follows:—

19 cases connected with and influenced by lesions in the nervous centres; under this class I include the insane.

19 cases connected with and influenced by the presence of a dyscrasia, such as typhus fever, variola, tuberculosis.

1 case connected with and influenced by arterial obstruction, causing pressure upon the entire mass of the affected parts, and total absence of circulation in the part.

The frequency with which lesions of the lung co-exist and succeed to disease of the brain, renders it at once apparent that the condition of the lung is materially affected by the influence of the nervous centres. In the cases recorded by Andral and Bright, diseases of the lung frequently going on to gangrene were often the immediate cause of death in patients suffering from cerebral disease; and it was also observed that the tendency to gangrene succeeding inflammation of the lung was promoted by the actual existence of disease in the brain. Cruveilhier has also directed attention to the frequency of gangrene of the lungs in epileptic subjects; and it has been remarked, that the insane are particularly prone to the disease, more especially when the bodily health has suffered, or where, as in maniacs, a greatly-depressed state of the animal functions succeeds to inordinate nervous excitement.*

In conclusion, allow me to state what I consider has been illustrated by the cases I have related in this paper. They show, 1st, That extensive lesions generally depend in part upon some morbid condition of the blood, existing either from alteration in its normal constitution, or from the presence of a morbid material. 2d, That such morbid conditions of the blood exercise an influence in modifying the elementary forms of organization of the exuded *liquor sanguinis*, the great tendency of which is to become organized in forms varying with the existing dyscrasia, and tending, least of all, to disintegrate or to involve the texture of the lung itself in death. 3d, That during the progress of typhus fever the exudation of *liquor sanguinis* in the lung assumes a low type of organization.

* Guislain, Gaz. Med. 1838. No. xxviii.

4th, That contiguous tissue exercises an influence upon the elementary forms which the exuded products assume. 5th, That any amount of texture may be involved. 6th, That the intervesicular-filamentous tissue, as well as the pulmonary vesicles, are the seat of the exudation. 7th, That in gangrene of the lung every simple element of the pulmonary tissue is involved. 8th, A deposition of fat in the lung I have also attempted to explain; and, 9th, I have shown that it is a morbid condition by no means uncommon; that it is found in conditions of obstruction to the respiratory process, and that it continues to accumulate until disintegration of the exuded products and death of the pulmonary texture. 10th, That pulmonary gangrene, along with death of the exuded matter, is connected with, and influenced by, lesions in the nervous centres, by the dyscrasia existing during typhus fever, variola, and tuberculosis, by arterial obstruction, causing pressure upon the entire mass of the affected parts, and total absence of circulation in the part.

EXPLANATION OF THE PLATES.

Plate I.

Fig. 1. Pavement epithelium from mucous membrane of smaller bronchia (after Lebert).

Fig. 2. Intermediate forms of epithelium, between the pavement, cylindrical, and vibratile (after Lebert).

Fig. 3. Valentin section from lung in Case 1. Compound granular corpuscles and granules amongst the fibres, and filling the air-cells; fibres unbroken.

Fig. 4. (*a*) Compound granular corpuscles; (*b*) colourless cells; (*c*) oil or fat; (*d*) blood discs and granular matter from fluid in the same lung.

Fig. 5. Pyoid corpuscles, colourless cells, and granules from fluid in lung of Case 2.

Fig. 6. Valentin section of same lung, showing fibrinous exudation and fibro-plastic cells, with pyoid and colourless corpuscles.

Fig. 7. Pus and oil globules from fluid of the grey part of lung in Case 3.

Fig. 8. Organized forms in fluid of the lung as it passes from red to grey. (*a*) Compound granular cell (few of them seen); (*b*) blood discs in masses; (*c*) colourless cells; (*d*) pus-corpuscles of the usual forms; (*e*) pus-corpuscles surrounded by a pellucid cell wall, within which the pus cells seem to float from side to side.

Fig. 9. Atheromatous deposit from the anterior tibial artery, composed of fat, crystals, and granules.

Plate II.

Fig. 1. Section of lung in Case 3, showing the pulmonary fibres separated very much, but not broken, intermingled with exuded matter, consisting of blood in masses, pus cells, oil globules and fat granules.

Fig. 2. Section from grey portion of same lung; no compound granular cells; every interspace filled with pus cells and oil; fibres much separated, but unbroken; no blood.

Fig. 3. Effect of acetic acid in bringing the vestiges of the form of air cells into view, showing the pus-corpuscles and granules, with the pulmonary fibres; no compound granular corpuscles.

Fig. 4. Exuded products in the form of the compound granular cell in passing from the grey to the red part.

Fig. 5. Appearances in Case 5; the more vascular part contained blood and imperfect cells, granular exudation, and fat.

Fig. 6. Granular exuded products, fat and oil drops in a section of the same.

Fg. 7. Exuded matter from gangrenous cavity in Case 7. (*a*) Oil globules and fatty granules; (*b*) pus-like cells; (*c*) blood discs; (*d*) compound granular cells, modified by the typhous dyscrasia. Broken-down fibres are interspersed.

Fig. 8. Contents of the millet-seed-shaped bodies, consisting of oil, compound granular masses, and pus cells, along with blood.

Fig. 9. The millet-seed-shaped bodies, the natural size, and magnified ten times.

Plate III.

Fig. 1. Valentin section from friable portion of lung surrounding the gangrenous cavity, in Case 7. Altered blood coloured the tissues; fibres unbroken; imperfectly-developed exuded material in masses modified by the typhous dyscrasia.

Fig. 2. Effect of acetic acid; cell-walls destroyed; appearances of fat and oil.

Fig. 3. Section of cartilage nodule in lung.

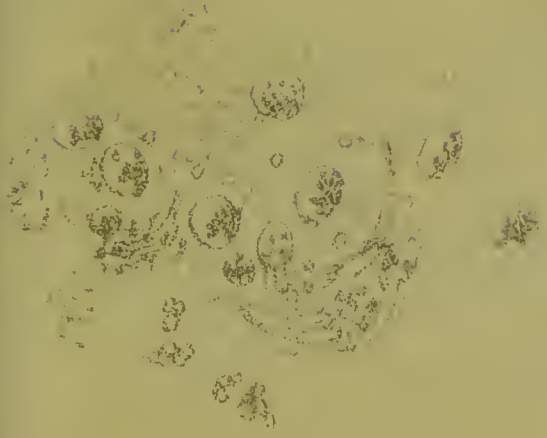
Fig. 4. Fluid from lung in Case 4. (*a*) Pus in various forms; (*b*) various forms of epithelium; (*c*) vibrions (?); (*d*) granules of fat.

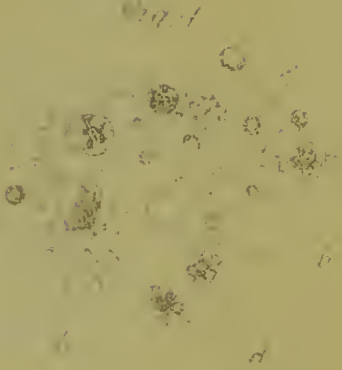
Fig. 5. Effects of acetic acid on the same fluid.

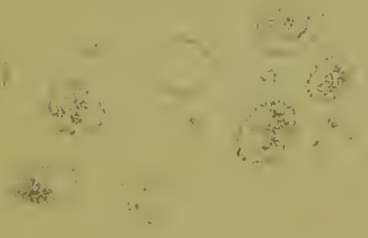
Fig. 6. Vibriones (after Lebert).

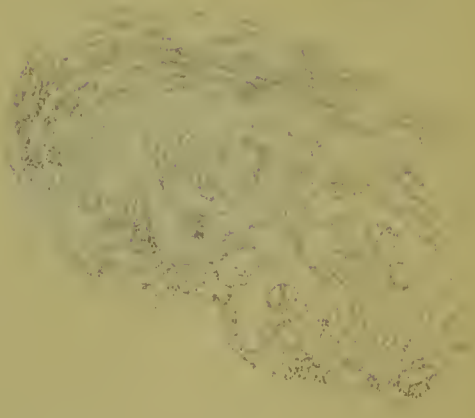
W. A.

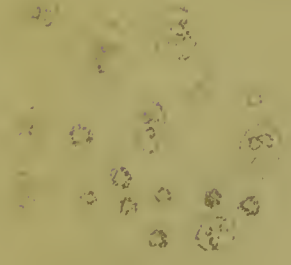
Note.—The microscopic observations were made with one of "Oberhausser's" microscopes ("Place Dauphine, 19, Paris"), and with a power of 250 or 300 diameters, unless otherwise mentioned.

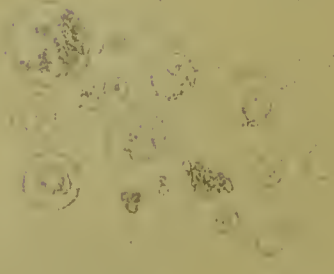












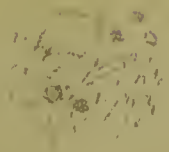


Fig 1

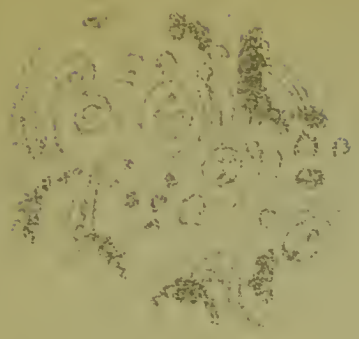


Fig 2

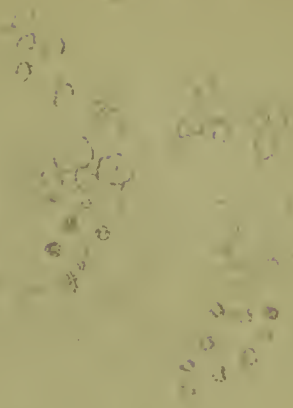


Fig 3

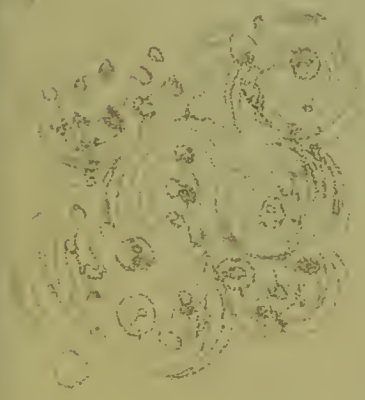
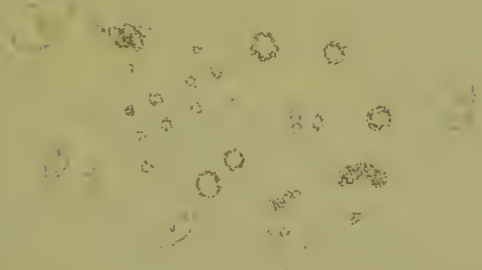
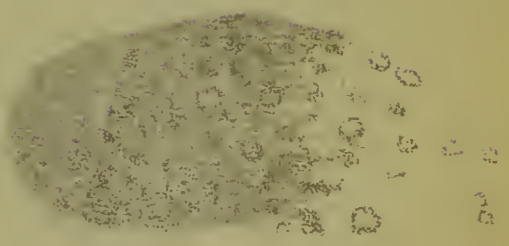


Fig 4





a

b

d

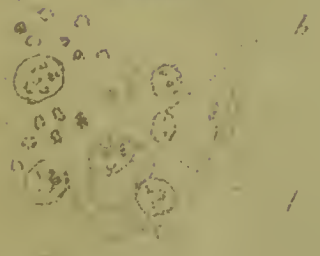


Fig 5

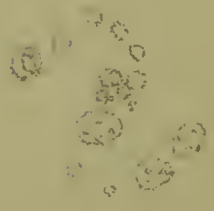


Fig 6

Fig 1

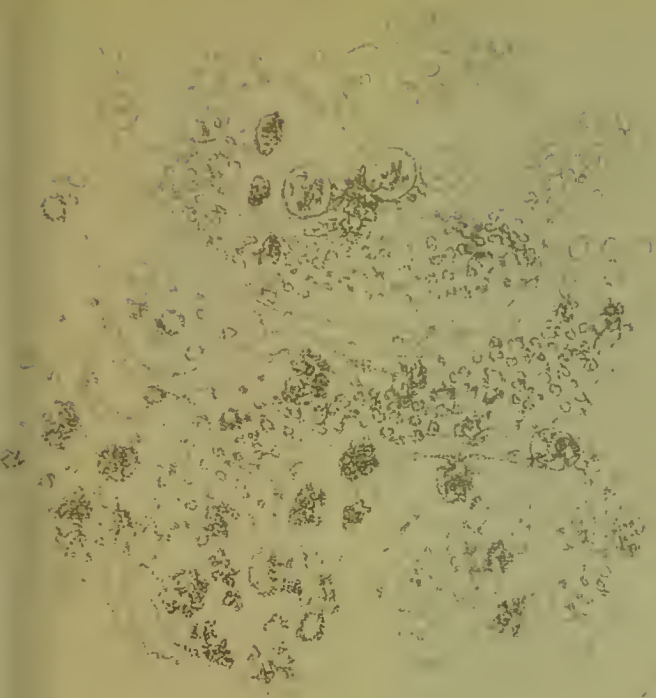


Fig 2

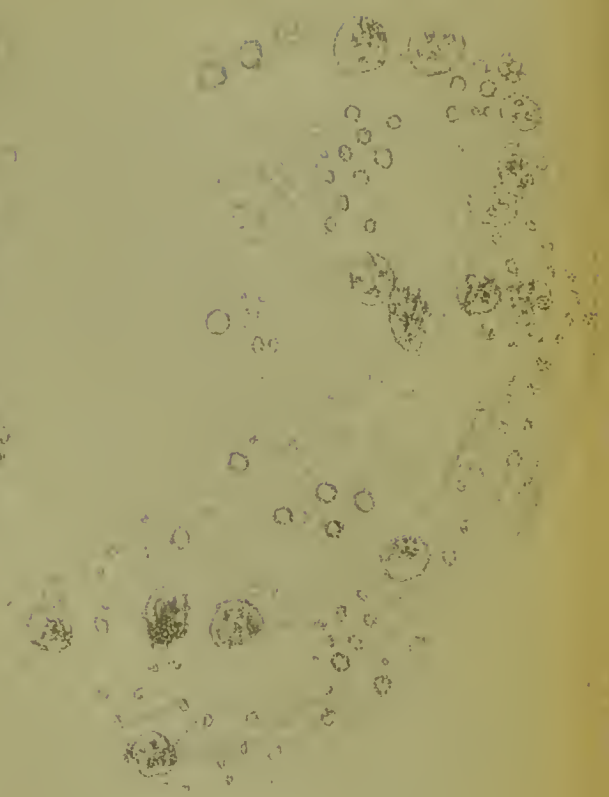


Fig 3

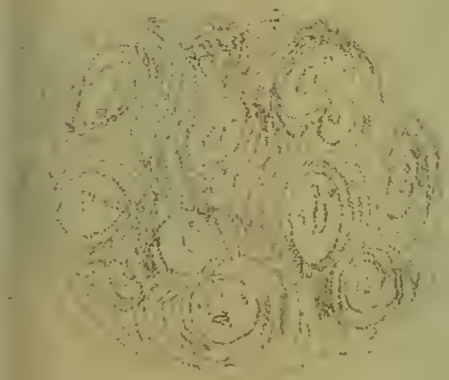


Fig 4

Fig 5

Fig 6